

THE *American Journal* OF *Gastroenterology*

VOL. 33, NO. 2

FEBRUARY, 1960

A Critical Review of 900 Cases
of Gastroduodenal Surgery

Tranquilizers and Gastric Secretion

Sublingual and Suppository Therapy
in Internal Medicine

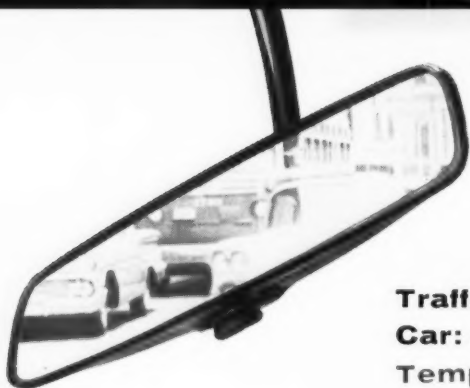
Malignant Degeneration in Chronic Inflammatory
Disease of the Colon and Small Intestine

Twenty-fifth Annual Convention
Philadelphia, Pennsylvania
23, 24, 25, 26 October 1960



Official Publication

AMERICAN COLLEGE
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Traffic: jammed

Car: stalled

Temper: mild

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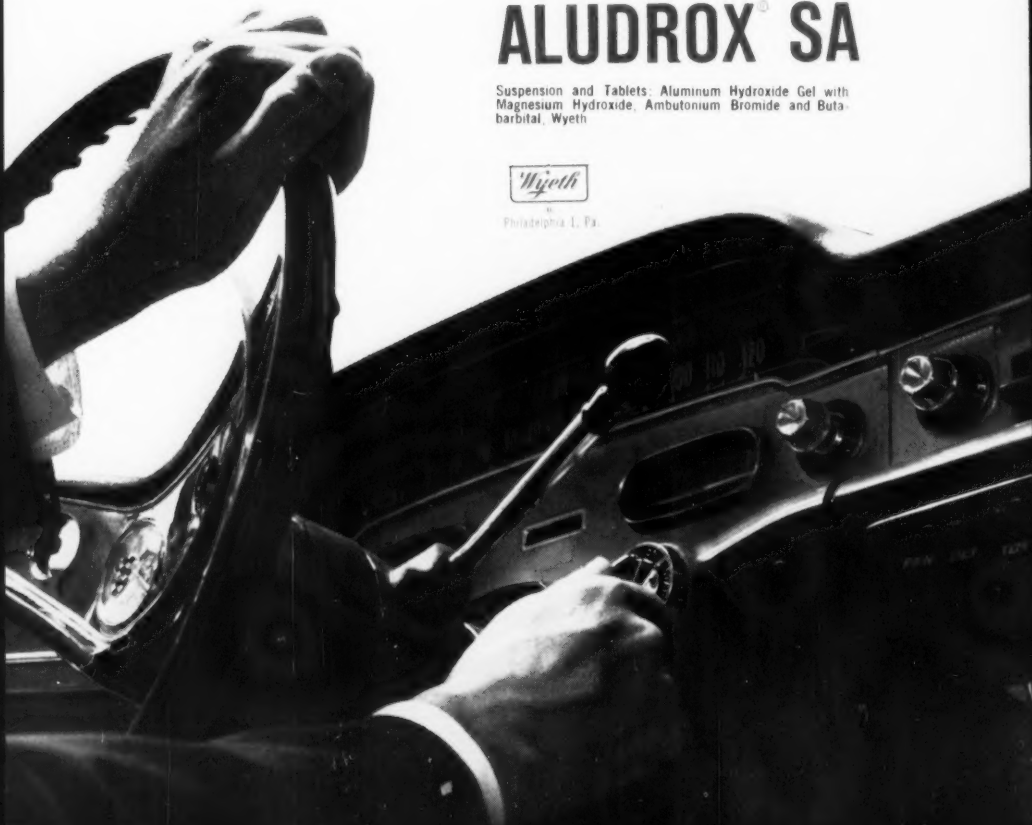
eases tension • promotes healing
relieves pain • reduces acid
secretion • inhibits gastric motility

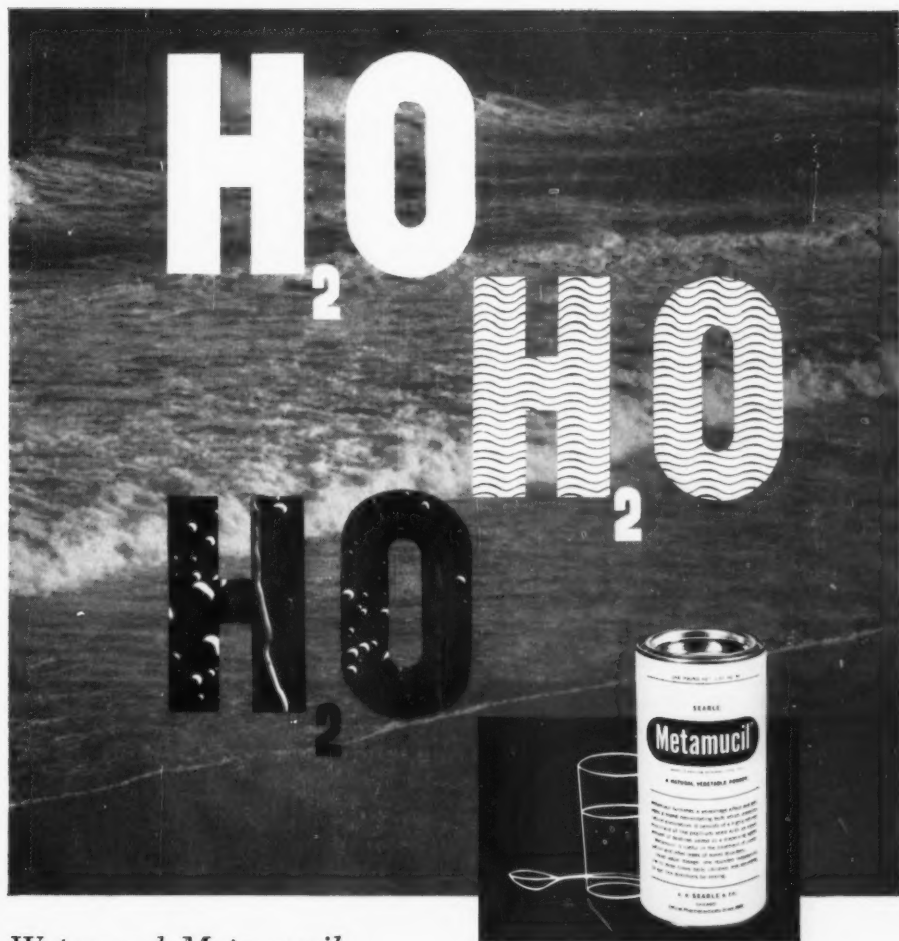
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THE American Journal OF Gastroenterology

(FORMERLY THE REVIEW OF GASTROENTEROLOGY)

*The Pioneer Journal of Gastroenterology, Proctology
and Allied Subjects in the United States and Canada*

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gastritis
esophageal spasm
intestinal colic
functional diarrhea
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DIAGNOSIS	No. of Cases	EFFECTIVENESS				SIDE EFFECTS				
		Marked Improvement	Slight Improvement	None	Percentage of Effectiveness	Transient Drowsiness	Dry Mouth	Visual Disturbances	Allergic Reaction	None
ULCER, DUODENAL	48	45	2	1	97.9%	6	1	1	—	41*
ULCER, GASTRIC	21	14	6	1	95.2%	2	1	—	—	18
GASTRITIS (acute, chronic) hypertrophic, alcoholic)	42	34	6	2	95.2%	6	1	—	—	36*
CHOLECYSTITIS (acute, chronic)	8	3	4	1	—	1	—	—	—	7
ESOPHAGOSPASM	4	3	1	—	—	1	—	—	—	3
CARDIOSPASM	3	2	—	1	—	—	1	—	—	2
PYLOROSPASM	14	11	3	—	100.0%	2	—	—	1	11
BILIARY DYSKINESIA	3	2	—	1	—	—	—	—	1	2
PSYCHOPHYSIOLOGIC GASTRIC REACTION (Gastritis Nervosa, Nervous Stomach, Hypermotility, Hyperacidity, Climacteric)	49	34	13	2	95.9%	5	3	—	—	41
ANXIETY STATES WITH G. I. DISTURBANCE	24	13	7	4	83.3%	1	—	1	—	22
TOTALS	216	161	42	13		24	7	2	2	103
PER CENT		75%	19%	6%	94.0%	11%	3%	.9%	.9%	84%

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CONCLUSIONS — The great predictability of effectiveness and the low incidence of side effects make Milpath of great value in the treatment of gastrointestinal diseases, whether organic or psychophysiologic in nature.

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Reference:

1. Whitehouse, W. M. & Fink, A. E., Med. Bull. Univ of Michigan 25:238, July 1959

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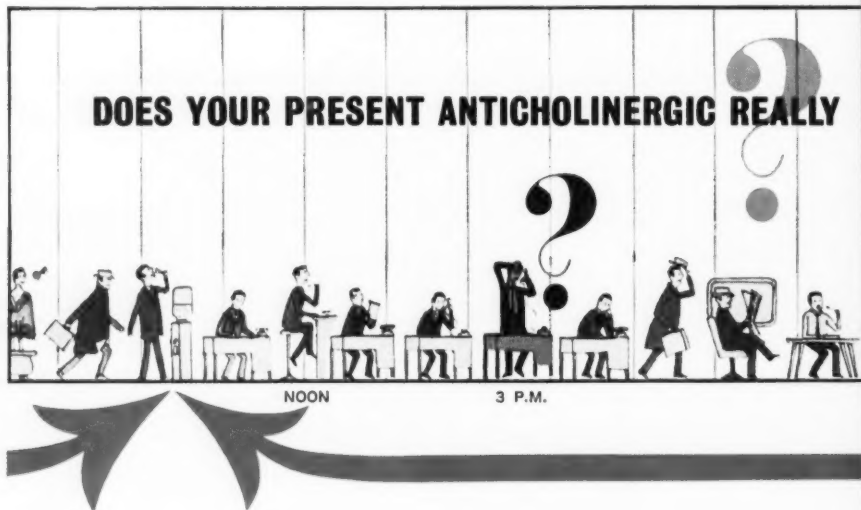
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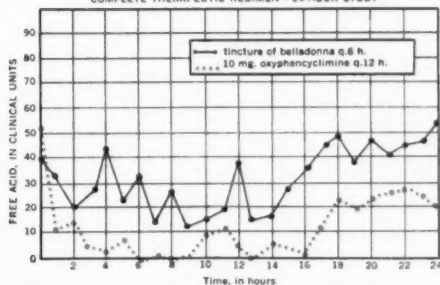


MIDNIGHT

2 A.M.

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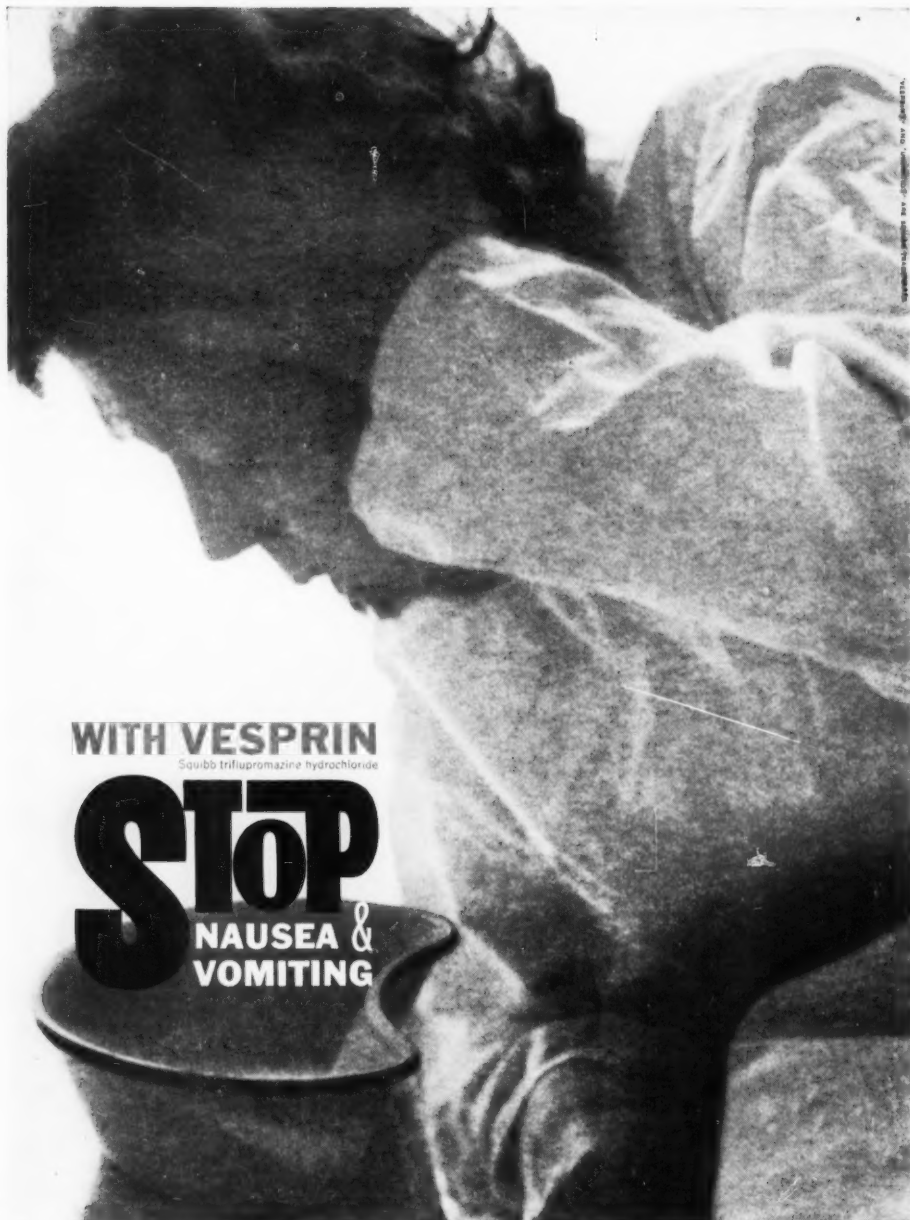
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References: 1. McHardy, G., et al.: J. Louisiana M. Soc. 111:290 (Aug.) 1959. 2. Steigmann, F.: Study conducted at Cook County Hospital, Chicago, Illinois, in press. 3. Kemp, J. A.: Antibiotic Med. & Clin. Therapy 6:534 (Sept.) 1959. 4. Leming, B. H., Jr.: Clin. Med. 6:423 (Mar.) 1959. 5. Data in Roerig Medical Department files.



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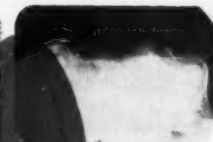
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12

vertical cassette stand used to support slow non-screen film exposed to low kV x-rays. (Details: 36-42 kV,

similar technique is used to demonstrate tissue destruction, pus pockets etc. To avoid interference from smears of opaque on wrapped film when the treated part is brought into contact with it, the Microtome Microopaque must be allowed to dry.

Two films which simulate successful repair of a cleft palate.

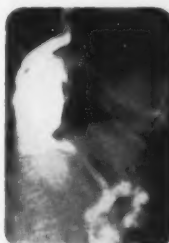
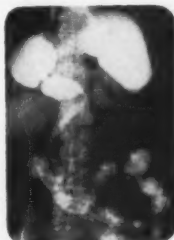


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With a nasal syringe, Micropaque (or Standard Mix on page 13) is conveyed via the nostril to the back of the nose and the patient instructed to swallow. It is useful to use for comparison similar films of normal subjects.

1

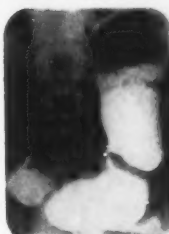
Two views of a completely thoracic stomach. The greater curvature is uppermost and the duodenal cap lies in the position of the *flexa*.



The amputating team was not delayed and it had apparently functioned normally during the long election. The patient (female) was 81 when examined.



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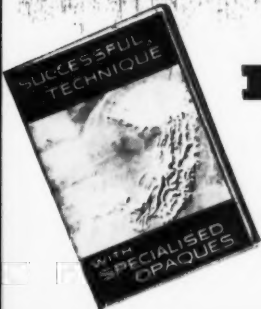
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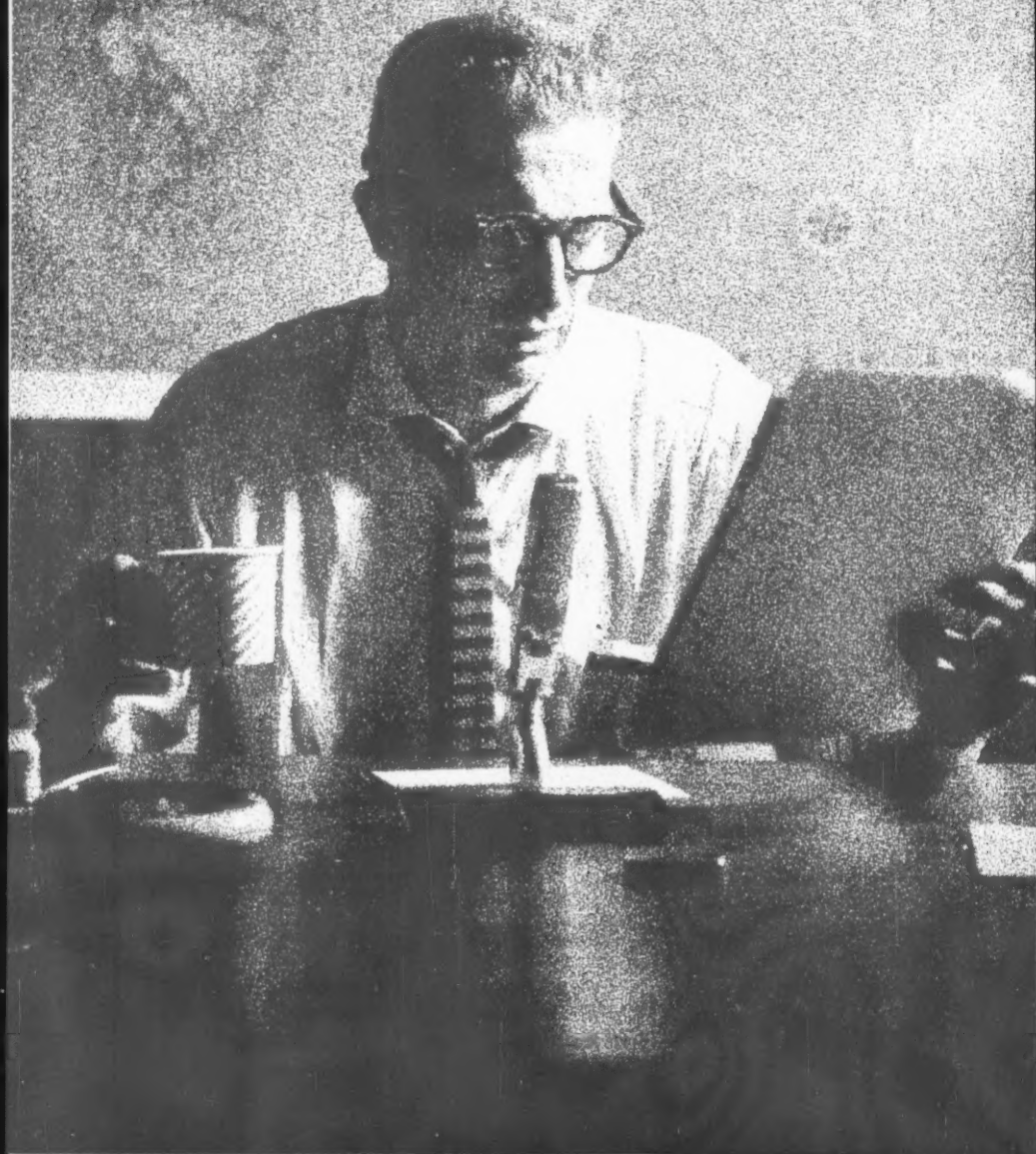
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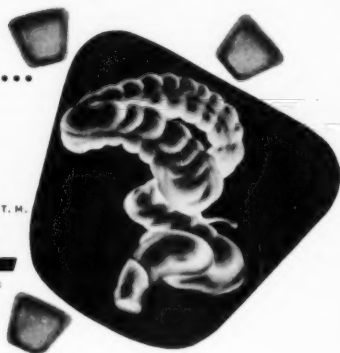
new concept for chronic constipation...

and especially that associated
with the irritable bowel syndrome

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safe, gentle transition
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A CRITICAL REVIEW OF 900 CASES OF GASTRODUODENAL SURGERY*†

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Gastroduodenal ulcers present a constant challenge to the practicing surgeon. Differences of opinion as to the ideal procedure for treatment of this prevalent condition continue to be expressed. Such lack of agreement suggests that there is, as yet, no ideal surgical procedure. Our purpose in this presentation, however, is to show the results of a large series of operations which indicate with increasing evidence the superiority of subtotal gastrectomy with vagectomy over the other presently available operations for treatment of the usual benign peptic ulcer.

This report encompasses an unselected series of 906 consecutive cases of gastroduodenal surgery performed by a private medical group during the 26-year period from 1933 through 1958. Cases were studied in terms of indication for surgery, operative procedure performed, operative mortality, and therapeutic result. The data was compiled from analysis of questionnaires and direct office follow-up.

Cases of gastric carcinoma are mentioned, but the primary study is that of peptic ulcer. Only apparently resectable cases of gastric carcinoma were included in this series, and exploratory laparotomies, in which inoperable carcinoma was found, are not tabulated. Bleeding esophageal varices were also not included. Included without special study were ten infants with hypertrophic pyloric stenosis, upon whom pyloromyotomies were performed, and one infant with an annular pancreas treated by duodenoduodenostomy.

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RESULTS OF STUDY

Tables I through VII show the composite results of the analysis of each individual case. A tabulation of the findings and courses of the nonsurvivors is given in Table VII.

Indications for surgery (Table I):—The two major categories of pathology requiring surgical treatment were gastroduodenal hemorrhage and intractable duodenal ulcer which failed to respond to adequate medical management. These were relatively close in frequency of distribution and together accounted for over 60 per cent of the cases in this series.

TABLE I
INDICATIONS FOR SURGERY

	Cases	% of total
Bleeding	312	34.4
Massive, requiring emergency surgery	69	7.6
Controlled and then elective surgery	243	26.8
Intractable duodenal ulcer	249	27.5
*Gastric ulcers (benign)	120	13.3
†Perforation of ulcer	92	10.2
‡Neoplasms	75	8.3
Malignant	73	8.1
Benign (leiomyomas)	2	0.2
§Pyloric obstruction	60	6.6
Marginal ulcer (uncomplicated)	19	2.1
Obstruction of gastrojejunal loop	3	0.3
¶Miscellaneous	6	0.7

*Including 22 operated for hemorrhage.

†Perforations include 1 gastric carcinoma and 1 marginal ulcer.

‡Total neoplasms include 8 carcinomas in which gross bleeding occurred, 1 perforated gastric carcinoma and 1 leiomyosarcoma.

§Pyloric obstructions include 10 infants and 1 adult with hypertrophic pyloric stenosis.

¶Include 1 gastrojejunal fistula, 1 tracheoesophageal fistula, 1 annular pancreas, 1 case bleeding varices and 2 cases of trauma.

Hemorrhage:—Hemorrhage, as an indication for surgery, was divided into two categories: massive uncontrollable hemorrhage, and hemorrhage which responded to transfusion and conservative therapy, but recurred in a few days, or recurred later in spite of medical management. Massive hemorrhage is defined as bleeding in which hemodynamic balance could not be obtained with rapid transfusion through several ports, or in whom administration of 2,000 c.c. of whole blood in any single 24-hour period failed to produce evidence of cessation of bleeding and/or improvement in clinical condition. These were operated

as emergencies. Out of 69 such cases, there were 12 deaths. This gave a mortality rate of 17.4 per cent in this group. This disturbingly high mortality, however, compares with other reports of large series^{1,4,7,8}, where the mortality rate in surgery on actively bleeding ulcers is from 7 to 23 per cent with an average of about 18 per cent. This is in marked contrast with the second group where

TABLE II
DISTRIBUTION OF OPERATIVE PROCEDURES

Operation performed	Number of cases		
	Male	Female	Total
Subtotal gastrectomy	417	105	522
Subtotal gastrectomy with vagectomy	134	31	165
Gastroenterostomy	29	18	47
Gastroenterostomy with vagectomy	13	2	15
Pyloroplasty	11	1	12
Pyloroplasty with vagectomy	10	8	18
Vagotomy (1 thoracic)	4	5	9
Total gastrectomy	8	3	11
Closure of perforated ulcer	82	10	92
*Miscellaneous	11	5	16
Totals	716	190	906
*Miscellaneous operations			Am't
Gastrotomy with ligation of bleeder			5
Gastrotomy			1
Detorsion of gastroenterostomy (previous gastrectomy with vagectomy)			1
Detorsion of gastroenterostomy with enteroenterostomy (previous gastrectomy with vagectomy)			2
Repair of gastrojejunal fistula			1
Wedge resection of stomach			1
Transection of stomach and resuture (bleeding varices)			1
Proximal gastrectomy and pyloroplasty			1
Pyloroplasty and repair of tracheoesophageal fistula			1
Devine exclusion with later antrectomy and vagectomy			1
Duodenoduodenostomy (annular pancreas)			1
			16

hemorrhage could be controlled by transfusion and conservative management, and surgery then performed with the patient in better condition. In this latter group, there was no differentiation from those treated electively for other reasons, and there were only two deaths out of an electively operated group of 243 patients for a mortality rate of 0.8 per cent in the group.

As others^{2,3,7} report, we feel that best control of hemorrhage is obtained by early and generous transfusion to restore normal circulating blood volume. Earlier ideas that raising blood pressure by transfusion would cause resumption of bleeding have been invalidated. The high mortality in massive hemorrhage appears to be primarily due to the magnitude of the initial disturbance of body physiology, particularly hepatic anoxemia, and where this imbalance can be corrected before surgery, the outcome is markedly improved. When, however, blood loss is overwhelming and not promptly controllable, prolonged conserva-

TABLE III
OPERATIVE MORTALITY

	Deaths	Cases in group	% mort. in group
Massive hemorrhage (emergency surgery)	12	69	17.4
Subtotal gastrectomy	9	61	14.8
Subtotal gastrectomy plus vagectomy	1	6	16.7
Resection of gastrojejunostomy (marginal ulcer after gastrectomy)	1	1	
Laparotomy for bleeding gastric ulcer (surgery not completed—card. arrest)	1	1	
Elective surgery for ulcer	5	609	0.8
Subtotal gastrectomy	3	368	0.8
Subtotal gastrectomy plus vagectomy	2	151	1.3
Gastroenterostomy with or without vagectomy	0	54	0
Pyloroplasty with or without vagectomy	0	19	0
Vagectomy	0	9	0
Miscellaneous (see Table II)	0	8	0
Gastric malignancy	8	73	11.0
Subtotal gastrectomy	3	57	5.3
Total gastrectomy	4	15	26.7
Closure of perforated gastric carcinoma	1	1	
Closure of perforated benign ulcers	4	91	4.4
Over all mortality including carcinoma	29	906	3.2
Over all mortality excluding carcinoma	21	835	2.5

tive efforts are not only fruitless, but allow further deterioration of the patient's condition with ammonia intoxication from intestinal absorption along with liver damage. Therefore, when massive uncontrollable hemorrhage is found, early surgical intervention is imperative. This policy has been generally adopted of late, and most surgeons have tended toward earlier operation.

Intractable duodenal ulcers:—Intractable ulcers were referred by internists after failure of conservative management, with persistent pain and disability.

A few patients, whose emotional environment precluded success of conservative therapy, and in whom a change of this environment was not feasible, were also subjected to surgery. Mortality rate, as indicated above, was a very satisfactory over all rate of 0.8 per cent, and was, of course, even less in the younger, better risk patients.

Gastric ulcers:—Gastric ulcers diagnosed on x-ray, including benign and malignant, totalled 156 and made up 17.3 per cent of the cases. Of these, 120 were benign and 36 malignant. Twenty-seven, including 5 carcinomas, were

TABLE IV
SURGERY ON PATIENTS PREVIOUSLY OPERATED FOR SAME CONDITION

Previous surgery	Later procedure	No. of cases
Closure of perforation	Subtotal gastrectomy	19
	Subtotal gastrectomy with vagectomy	7
	Gastroenterostomy with vagectomy	3
	Pyloroplasty with vagectomy	1
	Closure of perforation	4 34
Gastroenterostomy	Subtotal gastrectomy	6
	Subtotal gastrectomy with vagectomy	3 9
Gastroenterostomy with vagectomy	Subtotal gastrectomy	1
Pyloroplasty	Subtotal gastrectomy	1
Pyloroplasty with vagectomy	Subtotal gastrectomy	1
Vagectomy	Subtotal gastrectomy	1
Subtotal gastrectomy	Vagectomy	8
	Closure of perforated marginal ulcer plus vagectomy	1
	Repair of gastrojejunal fistula plus vagectomy	1 10
	*Enterointerostomy	2
Subtotal gastrectomy with vagectomy		

*For torsion and obstruction of efferent jejunal loop.

operated because of hemorrhage. The 98 benign gastric ulcers without hemorrhage were operated basically because x-rays indicated their presence. Gastric ulcers were rarely treated conservatively, but were generally considered potentially malignant regardless of location, and if the patient's condition permitted, were usually operated promptly. This policy was furthered by our findings of malignancy in over 20 per cent of gastric ulcers in our series. Of the operative deaths, six occurred in patients with benign gastric ulcers. Of these, two were elective operations, three were operated for massive hemorrhage, and one was perforated.

Perforated peptic ulcers:—Of the 92 perforated ulcers in this series, five died. Four of these were peptic ulcers and one a perforated gastric carcinoma who died eight days postoperatively largely as a result of carcinomatosis. This gave a net mortality in surgically treated perforated peptic ulcers of 4.4 per cent which compares favorably with reports from other series^{5,6}. Three cases were treated by immediate subtotal gastrectomy. One of these was a gastric ulcer which perforated while the patient was in the hospital and was operated within two hours of perforation. The other two were large gastric perforations in which the defect was too large to close. (All of these did well.) Four cases

TABLE V
AGE AND SEX DISTRIBUTION

Sex	Age range	Average	Mean deviation
Male	14 days to 87 years	54.1 yrs.	9.6 years
Female	4 days to 79 years	51.8 yrs.	8.7 years

Sex Distribution (Number of Cases)

Males716(79%), Females190(21%), Total906

Age Distribution

Age (years)	No. of cases	% of total
Under 20 (infants)	11	1.2
20 - 29	7	0.8
30 - 39	103	11.4
40 - 49	233	25.8
50 - 59	267	29.4
60 - 69	194	21.4
70 - 79	89	9.8
80 - 87	2	0.2

were treated by simple closure plus gastroenterostomy because of pyloric stenosis. Of the remaining 76 cases treated by simple closure, four reoperated a second time three to six years later and two of these plus 30 others required more definitive surgery six weeks to six years later. Forty-eight cases of perforation who had simple closure have not required further surgery to date. Thus, slightly over half of the perforated ulcers were amenable to medical management after simple closure.

Neoplasms:—Only two of the neoplasms on whom resection was performed were benign and both of these were leiomyomas. The mortality rate of 11 per cent in resection for carcinoma was largely because of the magnitude of the

surgery performed, with 11 total gastrectomies, extensive resection in most of the others, and removal of spleen, omentum, and occasionally part of the pancreas in a large proportion of the cases. It is of interest to note that almost one-third of the gastric carcinomas operated were in women.

Pyloric obstruction:—The 60 cases of pyloric obstruction, although demanding prompt intervention, presented no instantaneous need for emergency surgery, and since they could be prepared preoperatively by nasogastric suction, replacement of fluid and electrolytes, and other measures, most became relatively elective procedures. This is reflected in the absence of any operative mortality in this particular group. The ten infants and one adult with classical

TABLE VI
POSTOPERATIVE RESULTS

Operation	% of Patients in Group																	
	Subjective evaluation				Vomiting				Diarrhea				Dumping				Wt.	
	Excellent	Good	Fair	Poor	None	Mild	Moderate	Severe	None	Mild	Moderate	Severe	None	Mild	Moderate	Severe	Incr. or unchanged	Decreased
Gastrectomy	60	19	11	10	81	17	2	0	91	6	2	1	83	9	3	5	54	46
Gastrectomy and vagectomy	55	15	9	10	81	17	0	1	59	25	8	7	76	15	2	7	37	63
Gastroenterostomy and vagectomy	20	67	0	13	80	20	0	0	67	33	0	0	87	13	0	0	54	47
Pyloroplasty and vagectomy	45	33	11	11	89	11	0	0	83	17	0	0	83	17	0	0	67	33

hypertrophic pyloric stenosis were treated by Ramstedt pyloromyotomy, supplemented by vagectomy in the adult.

Marginal ulcers:—Of the 19 patients operated for gastrojejunal marginal ulcer, ten were present following subtotal gastrectomy, including one which perforated, and one which bled massively with fatal outcome in spite of surgery. Treatment of these consisted of vagotomy (thoracic in one, subdiaphragmatic in eight) plus simple closure of the one perforation. The remaining nine marginal ulcers operated followed earlier gastroenterostomy (one with vagotomy), and were treated by resection of the gastrojejunal anastomosis, enteroenterostomy, and subtotal gastrectomy, with vagotomy in three of the cases.

TABLE VII
DEATHS (SINCE 1947)

Year	Patient	Age	Sex	Indication for surgery	Course	Cause of Death
1947	M.L.	67	F	Perf. duodenal ulcer.	Had been perforated 4 days on admission.	Cardiac arrest when abdomen opened.
	O.D.	71	M	Ca. of stom. with reg. metast.	Subtotal palliative resection. Died 36 hours later.	Pulmonary edema and congest. heart failure.
1948	R.H.	70	M	Ca. of stom.	Total gastrectomy. Died 2 days postoperatively.	Pneumonia.
	J.S.	46	M	Massive hem. of duodenal ulcer.	Subtotal gastrectomy. Continued slow bleeding postoperatively. 6,000 c.c. of blood.	Myocardial infarction.
1950	E.B.	41	M	Massive hem. of marg. ulcer.	Previous subtotal gastrectomy. Massive bleeding (12,000 c.c. of blood). Re-resected.	Hemorrhagic shock.
	P.L.	53	F	3 prev. duodenal ulcer hemorrhages.	Subtotal gastrectomy. Operative B. P. fall to 40 mm. Hg. systolic. Died 14 days postoperatively.	Acute renal failure.
1953	H.C.	51	M	Massive hem. of duodenal ulcer.	Subtotal gastrectomy. 4,000 c.c. of blood. Postoperative leak of duodenal stump. Died 10 days postoperatively.	Rupture of congenital aneurysm of ant. inf. cerebellar artery.
	G.B.	71	F	Ca. of stom. with reg. metast.	Total gastrectomy. Died 2 days postoperatively with severe hyperthermia.	Possible cerebrovascular accident.
1954	T.R.	70	M	Massive hem. of gastric ulcer.	Admitted in shock with Hgb. of 4.0 gm. 11,000 c.c. of blood. Gastrectomy. Died 5 days postoperatively.	Pulmonary edema, cardiac failure.
	G.M.	75	F	Perf. gastric ulcer.	Late perforation. Closed. Died 36 hrs. postoperatively.	Postoperative shock.
	J.P.	64	M	Massive hem. of gastric ulcer.	Massive bleeding 6,500 c.c. blood. To surgery in shock. Gastrectomy begun but not finished.	Hemorrhagic shock, cardiac arrest.

1955	W.S.	61	M	Leiomyosarcoma of stom. with metastasis.	Palliative resection. Died 14 days postoperatively.	Lower nephron nephrosis.
1956	E.P.	52	M	Ca. of esophagocardiac junction.	Total gastrectomy with interposition of jejunal segment between esophagus and duodenum and reanastomosis of jejunum. Died 5 days postoperatively.	Obstruction of lowest anastomosis and leak of upper one.
	E.N.	68	M	Gastric ulcer.	Subtotal gastrectomy. Died 5 days postoperatively.	Perf. duodenal stump.
	F.E.	62	M	Massive hem. of duodenal ulcer.	4,000 c.c. of blood. Subtotal gastrectomy.	Myocardial infarct. and congestive failure.
	M.Z.	57	F	Chronic duodenal ulcer.	Postoperative adhesive obstruction of efferent loop. Lysis on 28th day after gastrectomy. Reconstructed from foreign body giant cell reaction to catgut. Re-resected on 45th postoperative day and closed with silk.	Postoperative shock, pancreatitis, and cardiac failure.
1957	A.T.	64	F	Massive hem. of duodenal ulcer.	5,000 c.c. of blood given.	Postoperative pancreatitis.
	P.S.	62	M	Duodenal ulcer with many prev. hem.	4,000 c.c. of blood. Wound dehiscence on 8th postoperative day. Closed. Died 14 days postoperatively subtotal gastrectomy.	Pulmonary atelectasis.
	E.A.	55	F	Massive hem. of duodenal ulcer.	Hgb. 4.6 on admission. 3,500 c.c. of blood. Posterior ulcer in pancreas with pancreatic edema. Subtotal gastrectomy with vagectomy.	Necrosis of common bile duct with bile peritonitis and pancreatitis.
1958	A.B.	76	M	Perf. of ca. of stomach.	Generalized carcinomatosis with multiple complications. Died on 8th postoperative day after closure of perforation and liver biopsy.	Carcinomatosis, pulmonary infarction, atelectasis, pleural effusion.
	F.C.	54	M	Chronic duodenal ulcer.	Subtotal gastrectomy and vagectomy. Died 4th postoperative day.	Cardiac failure. Possible duodenal stump leak.

Obstruction of gastrojejunal loop:—Although there were no recurrences of ulcer following gastrectomy with vagectomy in our series, one postoperative complication occurred in three of these cases. This was torsion and obstruction of the gastrojejunal loop. Two of these were treated by detorsion and enterenterostomy, and one by simple detorsion. Since practicing suspension of the lesser curvature of the stomach to the stump of the round hepatic ligament and performing relatively routine anti-isoperistaltic gastrojejunostomy, we have had no further occurrences of this complication.

PROCEDURES PERFORMED

The main operative procedures employed were gastrectomy, gastroenterostomy, and pyloroplasty, all with or without vagectomy, and of course, the closures of perforated ulcers. In the earlier years of this series relatively fewer gastrectomies and more gastroenterostomies were done and elective surgery was performed with greater reluctance. This was not because of appreciably greater mortality in the cases operated, which were generally less radical procedures, than now, but because of uncertainty of uniform therapeutic success, and because of greater postoperative morbidity with the lack of the present wide variety of antibiotics and other therapeutic aids. Fewer poor risk patients were then even considered for surgery. Our trend has been toward more liberal use of surgery in elective cases than in the past. Increasingly, we have used subtotal gastrectomy plus vagectomy as the usual procedure of choice for cure of peptic ulcer. In our hands, this has produced the greatest protection against recurrence.

TECHNIC

At present, with exceptions for unusual circumstances, all of the surgeons in our group generally perform gastrectomy with vagectomy by the general technic described earlier by one of us⁹.

Where configuration of the costal margin permits (costal angle not extremely narrow), a bilateral subcostal incision is utilized, dividing both recti, and if necessary, extending the incision into the obliques. This gives excellent exposure with minimal need for retraction, and yields a strong transverse closure. Subdiaphragmatic vagectomy is performed, removing segments of both vagi. Although the right or posterior vagal trunk is often somewhat separated from the lower esophagus and must be picked up on the left crus of the diaphragm, Burge and Clark¹⁰ in England feel that very high right vagal interruption is undesirable because some fibers of the right vagus descend on the crus of the diaphragm to the celiac plexus. Their studies suggest that adequate gastric denervation with avoidance of postvagotomy diarrhea is obtained by interruption of only the gastric branch of the right vagus with preservation of the celiac branch. High division is far more likely to divide the common trunk although

the level of bifurcation of the nerve is variable. (This, of course, does not explain the appreciable incidence of diarrhea after gastrectomy without direct vagotomy.) The esophagus is stripped cleanly around its circumference because there are often accessory smaller vagal trunks in addition to the standard two.

After the vagectomy, a $\frac{1}{2}$ to $\frac{3}{4}$ gastrectomy is performed with an antecolic anti-isoperistaltic Polya type of anastomosis. (A high resection is performed to provide greater assurance of lasting cure in case of regeneration of vagal fibers.) Open technic is used and anastomosis accomplished with a two-layer closure using continuous 3-0 chromic catgut sutures. Before performing the mucosal closure, the serosa of the stomach is cautiously incised, exposing the vessels in the gastric wall. These are individually clamped before division and ligated with 4-0 chromic catgut, giving effective hemostasis and minimal blood loss. The duodenal stump is closed in two layers, using continuous 3-0 chromic catgut for the first layer which is inverted by a second layer of interrupted mattress sutures of 3 or 4-0 silk. The lesser curvature of the stomach is then sutured to the stump of the round hepatic ligament to reduce upward pull on the afferent limb of jejunum and prevent kinking and torsion of the anastomosis.

Posterior gastrojejunostomy is done only if the transverse mesocolon is so long and heavy that anastomosis anterior to the colon would require too long a jejunal loop. If the greater omentum is very heavy, it is either split, partially resected, or posterior anastomosis performed. We have found no significant over all superiority in postoperative symptomatology of posterior over anterior gastrojejunostomy, and the latter is more easily and therefore more securely and rapidly performed. Many workers feel that posterior anastomosis lessens incidence of the dumping syndrome, but some studies¹¹ have shown a higher incidence of biliary vomiting with posterior anastomosis. Taylor¹², in England, feels that biliary vomiting, and to some degree the dumping syndrome, is often due to a kinked afferent loop junction with the stomach with transient filling of the afferent loop from obstruction, and then sudden release of a large amount of bile into the stomach as pressure builds up high enough to overcome the obstruction. We have usually been able to avoid this tight angulation by the simple expedient of pulling the lesser curvature of the stomach down and suturing it to the stump of the round ligament which was divided on entering the abdomen.

With regard to the use of a Polya rather than a Hofmeister type of anastomosis, we feel that dumping is not significantly altered. If more than 50 per cent of the stomach is removed, it no longer functions as a reservoir because of rapid emptying⁸. Creation of a narrow gastrojejunal orifice does not provide any actual valve, and the effective efferent stoma in a Polya anastomosis is not the gastrojejunal connection, but is the lumen of the jejunum at the point of departure of the efferent loop from the stomach. Thus, we find that a simple open two-layer continuous catgut closure of the Polya type is rapidly and easily performed, and gives results essentially as good as more complex and time-

consuming procedures. Danger of obstruction by stomal edema is minimized, and the dangerous angle at the junction of the anastomosis and the medial gastric closure of the Hofmeister procedure is avoided. In our approximately 650 closures by this method, there has not been a single instance of postoperative leakage of this anastomosis.

In benign gastric ulcers, the same technic may be used in the infrequent case with high acidity and night secretion. In the usual gastric ulcer with low acidity, however, similar gastrectomy is performed without vagectomy; and Hofmeister or other variations in technic are used, if necessary, to accomplish removal of the ulcer. A Billroth I type of gastroduodenostomy with vagectomy is done in some of these cases.

Gastroenterostomy with vagectomy is now usually reserved for the poor risk patient with obstruction or severe scarring of the duodenum.

Our experience with pyloroplasty and vagectomy has been limited to a rather small number of cases as yet, but since our recurrence rate of ulcers after this procedure has been over 10 per cent, and general averages of recurrence rate are reported as approximately 5 per cent¹³, we have been somewhat reluctant to use this procedure as a routine in good risk patients. We will undoubtedly use it more, however, in poor risk patients where a brief and less extensive procedure is desirable.

The only deaths in cases operated electively for ulcers occurred in patients undergoing gastrectomy (with or without vagectomy). Without vagectomy the mortality rate was 0.8 per cent and with vagectomy it was 1.3 per cent. These are both satisfactorily low, and the small difference seemed to be more related to the individual cases involved than to any complications attributable to the vagectomy itself.

Fifty-nine of the patients operated in this series had undergone a previous surgical procedure for the condition. These are summarized in Table IV.

AGE AND SEX DISTRIBUTION

The total numbers of patients undergoing each operation and the age and sex distribution in the series is tabulated in Tables II and V. The ratio of males to females in our series was approximately 4:1 for almost all categories. In perforated peptic ulcers, where the ratio was 8:1, it still indicates an appreciable incidence of this condition with perforation of about one out of 17 ulcers operated in females. Carcinomas, surprisingly, were only twice as common in men as in women.

Excluding the infants (with no ulcers), the age range was 20 to 87 years with the median in males of 54.1 years being slightly above that of 51.8 years for females. Even though the greatest incidence of disease was in the sixth

decade, it is of interest to note that over 30 per cent of the patients in this series were beyond 60 years of age and almost 10 per cent were over 70.

THERAPEUTIC RESULTS

Subjective evaluation of results of surgery by a group comprised of ulcer patients, who, almost universally, have an emotional problem, always introduces factors which are not basically related to the surgery performed. Functional digestive difficulties which are not actually a part of the gastritis-ulcer syndrome, may not be eradicated by gastroduodenal surgery. The patient who has always complained of gas and problems of elimination may tend to consider their persistence after surgery as an indication that the surgery was not completely successful since it did not eradicate all of his symptoms. Some patients implicated the surgery in describing any and all symptoms arising subsequent to gastrectomy including menopausal hot flashes, headaches, and even failing vision. It is interesting to note in replies to questionnaires that some patients, who obviously have some degree of dumping syndrome and/or diarrhea or vomiting, may evaluate the results of surgery as excellent, since they no longer have pain or bleeding, while others, who indicate that they do not have pain, bleeding, nausea, vomiting, diarrhea, or elements of the dumping syndrome, will consider the therapeutic results of surgery as only fair or even poor. It is important to explain to a patient about to have gastroduodenal surgery that improvement is to be expected, but that surgery will not necessarily produce a complete rejuvenation. It is often true that the most emotionally unstable, neurotic patient is the one most likely to have postoperative problems such as vomiting, diarrhea, or "dumping", although these symptoms can and do appear in some of the apparently well-adjusted individuals.

Since subjective evaluation is thus so variable and intangible, we have noted in Table VI not only the summary of patient evaluation of therapeutic results, but also the three important objective symptoms of vomiting, diarrhea, and the dumping-complex. Weight changes and percentage of recurrence of disease are also tabulated. It can be seen that little over all difference appears in the subjective evaluation of results of subtotal gastrectomy, subtotal gastrectomy with vagectomy, pyloroplasty with vagectomy, and gastroenterostomy with vagectomy. Seventy-five to 80 per cent of the patients in each group considered results to be good to excellent and around 10 per cent considered results poor. When, however, objective findings are compared there are more definite differences. Recurrence of ulceration or bleeding was highest in gastroenterostomy with vagectomy with 13.3 per cent, almost as high in pyloroplasty with vagectomy at 11.1 per cent, moderate in subtotal gastrectomy with 4.4 per cent, and zero in subtotal gastrectomy with vagectomy. This is somewhat counter-balanced by the figures indicating significantly greater incidence of diarrhea and dumping syndrome and greater weight loss in the last category with least disturbance of physiology in the groups with pyloroplasty or gastroenterostomy

(both with vagectomy). Fortunately, most of the severe symptomatology disappears or lessens in from three months to two years, but a few patients continue to have distressing symptoms indefinitely.

COMMENT

Crile¹³, editorially, confirms the statement that gastrectomy with vagotomy gives better control than vagotomy with lesser drainage procedures. He discourages, however, routine performance of the more major operation, largely because of the high average mortality rate reported for elective gastrectomy elsewhere.

A recent survey¹⁴ in Ohio by the American College of Surgeons in 29 hospitals, regarded as being among the best in the state, showed a mortality in 2,562 elective operations for duodenal ulcer of 4.3 per cent. Eighty-nine per cent of the operations were performed by board-certified surgeons or Fellows of the American College of Surgeons. This did not include deaths following emergency operations for bleeding or perforation. The state-wide mortality for elective gastric resections was 4.9 per cent and that for lesser operation (mainly vagotomy with a drainage procedure) was 1.7 per cent.

Since our mortality rate for gastrectomy, using the procedure outlined, was only 0.8 per cent, and, even with added vagotomy, was only 1.3 per cent, Crile's major objection is eliminated. We feel, therefore, that in good risk patients, subtotal gastric resection with subdiaphragmatic vagectomy should be the procedure of choice among presently available technics for surgical cure of peptic ulcers. Discretion in very complicated ulcers and in poor risk patients would indicate election of a more conservative procedure such as vagotomy with pyloroplasty or gastroenterostomy in only those restricted circumstances.

SUMMARY

Nine hundred and six cases of gastroduodenal surgery are reviewed in terms of indication for surgery, operative procedures performed, operative mortality, and therapeutic result. The procedures primarily discussed were gastrectomy, pyloroplasty, and gastroenterostomy, with and without vagectomy, and closure of perforated ulcers.

The preferred operation for cure of benign peptic ulcer in this series was $\frac{3}{4}$ distal gastrectomy with antecolic anti-isoperistaltic Polya anastomosis plus subdiaphragmatic vagectomy. The technic usually employed by the authors is described and evaluated.

An over all operative mortality rate of 3.2 per cent was found, including all types of procedures and all diagnoses, including gastric carcinoma. When carcinoma is excluded, the over all mortality dropped to 2.5 per cent. Mortality for elective subtotal gastrectomy for benign gastroduodenal ulcer was 0.8 per

cent and that for subtotal gastrectomy with vagectomy done electively for ulcer was 1.3 per cent.

There were no recurrences of ulcer after subtotal gastrectomy with vagectomy, 4.4 per cent after subtotal gastrectomy without vagectomy, and 11.1 and 13.3 per cent respectively after pyloroplasty and gastroenterostomy both with vagectomy. Postoperative vomiting, diarrhea, dumping syndrome, and weight loss, however, were in general all inversely proportional to the recurrence rate.

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TRANQUILIZERS AND GASTRIC SECRETION*

WITH COMMENTS ON CLINICAL EXPERIENCE IN 60 CASES WHEN COMBINED
WITH ANTICHOLINERGIC DRUGS IN GASTROINTESTINAL DISEASE

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With the introduction and widespread use in the past five years of a whole spectrum of tranquilizers much interest has been directed to their effect on secretory activity. This interest was initially aroused when it became apparent that the first of these, reserpine, when given intravenously, proved to be one of the most potent short-term stimulants to the production of hydrochloric acid in the stomach^{1,2,3}.

A number of reports on harmful gastrointestinal complications following the use of reserpine in the therapy of hypertension then followed. An increased incidence and reactivation of duodenal ulcer with complications of perforation and hemorrhage were cited by additional observers^{4,5} during hypertensive therapy. The increase in volume and secretion, however, was later shown to be present only when the drug was administered in large doses and presently it was apparent that it could be used safely in patients with duodenal ulcer in therapeutic doses^{6,7}. Indeed following its administration in a series of cases of duodenal ulcer, one observer advocated its use as a valuable adjunct in therapy for ulcer^{7a}.

As each new tranquilizer appeared it was natural that studies on its effect on gastric secretion and motility would seem to be indicated so that its possible suitability for use either alone or in combination with anticholinergic drugs might be established for future clinical application in gastrointestinal problems. The enhancement of the known depressant action of anticholinergic drugs on gastric volume output by the possible additive inhibitory action of tranquilizing agents on gastric acidity was a possibility that appeared to merit investigation.

Recently we investigated the effect on gastric secretion of two tranquilizers: one a phenothiazine derivative, thiopropazate^{**}, and another, prochlorperazine†,

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**Thiopropazate-dihydrochloride (Dartal) G. D. Searle & Co.

†Prochlorperazine (Compazine) Smith, Kline & French Co.

alone and in combination with an anticholinergic drug, isopropamide*, in normal medical students. Concurrently over a period of 18 months we evaluated in a clinical study the usefulness of these medications in patients with peptic ulcer and related functional gastrointestinal disease. In the instance of thiopropazate it was used alone and also in combination with propantheline† in cases of gastrointestinal dysfunction when a prominent generalized psychophysiologic anxiety component was present clinically: while the prochlorperazine-isopropamide was administered in combination in a similar group of patients.

TABLE I
EFFECT OF THIOPROPAZATE ON TOTAL MEQ. ACID IN NORMAL HUMANS

Time	Drug Greater	Placebo Greater	Total Cases
Fasting specimen	6	6	12
15 minutes	7	6	13
30 minutes	5	5	10
45 minutes	6	8	14
60 minutes	5	7	12
75 minutes	3	11	14
90 minutes	2	10	12
105 minutes	3	8	11
120 minutes	1	8	9

Table indicating the significance of the data of the effect of a single dose thiopropazate (20 mg.) when taken orally by normal individuals on gastric secretion. The figures indicate the number of cases for which at a given time after administration the total mEq. acid exceeded that for the placebo compared with those for which the reverse was true. From the 5th observation on the drug consistently reduced total acid as compared to the placebo in a statistically significant manner.

The gastric secretory studies with both these agents will be presented in greater detail elsewhere³. The results of these findings will be summarized in this report and comparison will be made with the available data in the literature on the effect of these and other available tranquilizers on gastric secretory activity. Our clinical impressions of the value of the addition of these tranquilizers to the anticholinergics as utilized in peptic ulcer and related gastro-

*Prochlorperazine-isopropamide (Combid) Smith, Kline & French Co. Isopropamide is Darbid.

†Propantheline-thiopropazate (Pro-Banthine-Dartal) G. D. Searle & Co.

intestinal disturbances will be correlated with observations reported by other clinicians. From these combined observations some definite opinion and conclusions appear warranted at this writing.

MATERIALS AND METHODS

Thirty-two fractional gastric analyses were performed in the first part of our study. These consisted of a comparison of the effect of thiopropazate dihydrochloride on gastric secretion when ingested orally in the dose of 20 mg. taken with a small amount of water in normal individuals (16 medical students), as against the effect of an identical placebo in the same individuals on the following morning. The secretory volume, pH (using a Beckman pH meter) total mEq. acid/l., the free mEq. acid/l. and mg. HCl were obtained by the fractional method over a two-hour period one-half hour after the ingestion of the drug. Specimens were obtained by extraction every 15 minutes on eight consecutive occasions.

In the second part of our study, a comparison of the effect of a prolonged acting prochlorperazine-isopropamide combination on gastric secretion was carried out as against the prolonged-acting prochlorperazine alone and also against an identical placebo in the same group of normal individuals (25 medical students), on three different mornings one week apart three hours following the oral drug ingestion of a single dose. In all 71 gastric secretory studies were accomplished in this phase. The drug dosage consisted of 10 mg. and 5 mg. respectively of the prochlorperazine-isopropamide combined capsule in the form of a Spansule*. Similar secretory data was obtained by the fractional method over a two-hour period for thiopropazate.

The third phase of our study consisted of observations made on 60 cases of gastrointestinal disease over a period of two years, as a purely clinical portion of our study. These were diagnosed by definitive and appropriate x-ray and laboratory studies as duodenal ulcer, hypertrophic gastritis, symptomatic hiatus hernia with or without peptic esophagitis, (as established by x-ray and flexible open-tube esophagoscopy,) the irritable colon syndrome (with symptoms of generalized abdominal distress, nausea, vomiting, gaseous distention and alternating constipation and diarrhea) and nonspecific diarrhea. Included were three cases of the "dumping syndrome". The time of observation ranged from three weeks to three months in each patient.

The patients were divided into three groups: 1. Ten cases treated with thiopropazate alone (5 mg. t.i.d. and h.s.) were those in which the anxiety factor seemed equal to or even predominated over the gastrointestinal symptoms. 2. Twenty-five cases were treated with propantheline bromide 15 mg.-thiopropazate 5 mg. combined drug 12 hours apart as an adjunctive treatment

*Trademark SKF.

or as the only medication. The reaction of the patient whether excellent, good, fair or poor as well as the development of side-effects was noted at weekly intervals. 3. Twenty-five cases were treated with the sustained release prochlorperazine (10 mg.) isopropamide (5 mg.) preparation, 12 hours apart twice daily.

TABLE II
EFFECT OF PROCHLORPERAZINE-ISOPROPAMIDE ON MG. HCL

Time	Prochlorperazine-Isopropamide			Prochlorperazine			Placebo		
	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)
Fasting specimen	16	7	2	11	10	4	4	9	10 (-2)
15 minutes	11	12	1	10	9	4 (-1)	6	4	12 (-2)
30 minutes	11	7	3 (-2)	11	8	4	4	9	8 (-2)
45 minutes	6	11	4 (-2)	16	3	3	7	8	6 (-3)
60 minutes	11	10	1 (-2)	13	7	3 (-1)	6	8	8 (-2)
75 minutes	13	8	3	10	8	5	6	7	9 (-2)
90 minutes	14	7	2 (-1)	10	10	4	3	9	10 (-2)
105 minutes	15	6	2	8	10	6	4	8	10 (-2)
120 minutes	15	8	1	10	10	2 (-2)	5	7	10 (-2)
Total	112	76	19 (-7)	99	75	35 (-6)	45	69	83 (-19)

Effect of prochlorperazine-isopropamide on mg. HCl obtained by fractional gastric analysis in 25 normal medical students as compared to the effect on the same individuals one week apart of prochlorperazine and placebo (see text for comment).

- (1)—Incidence of lowest figure of mg. HCl.
 (2)—Incidence of middle figure of mg. HCl.
 (3)—Incidence of highest figure of mg. HCl.

(—) indicates number of specimens missing.

It is to be noted that the double-blind method with the use of placebo was not employed in this study. Since these patients were seen for many months before and after the observation period with the above drugs, other medications including other types of tranquilizer combinations were employed at

other time periods. An effort was made in the course of the observations to compare the effectiveness of the two combined tranquilizer-anticholinergic preparations.

RESULTS

Effect of thiopropazate on gastric secretion in normals:—In the 16 cases where secretion was studied in normal human subjects there was no comparable significant difference between the effect of a single dose of 20 mg. of thiopropazate taken orally in the first four specimens obtained at 15-minute intervals, when compared to the effect of a placebo. After the fifth specimen, however, total acid output was consistently reduced as compared to the placebo in terms of total mEq. acid. Table I indicates the number of cases for which at a given time after administration the total mEq. acid with the drug exceeded that for the placebo when compared for those for which the reverse is true.

Effect of prochlorperazine alone and with isopropamide on gastric secretion in normals:—In the analyses where prochlorperazine alone was compared with the prochlorperazine-isopropamide and a placebo, it was apparent that prochlorperazine when compared to the placebo alone had a significantly higher incidence of specimens with the lowest figures for mg. HCl. Following the administration of the combined form the lowest figures for mg. HCl occurred in five time periods out of nine; with the latter also the least number of specimens with the highest figures for mg. HCl occurred in eight of the nine time periods (See Table II and III).

In regard to volume and pH when the prochlorperazine is compared to the combined effective drug it appears on a study of the charts that no difference is present between the two and it is difficult in this instance to conclude what either have done to the secretion rates. It is to be emphasized that these subjects were supposedly normal and were not hypersecretors. In order to attempt to demonstrate an effect of an agent on gastric secretion it has been stated that it is best to choose patients with known duodenal ulcer or who are known hypersecretors in order to demonstrate suppression. Competent observers have shown, however, that isopropamide is an effective inhibitor of gastric secretion and motility^{14,15}; additionally, it has been reported that in human pharmacologic studies at experimental levels, prochlorperazine alone produces inhibition of gastric secretion²⁰. Our results indicate that the tranquilizer alone and the combined form administration are accompanied by significantly lower levels of acid than after giving the placebo.

Clinical effect of thiopropazate alone:—In most instances, the drug was given alone at periods other than when medication was taken for specific gastroenterologic problems. In others, the drug was given in conjunction with other agents, and the response was noted. Clinically, there appeared to be a definite calming effect in 60 per cent of the cases in doses of 5 mg. t.i.d. and

at bedtime. Of these, 10 per cent were clearly and effectively benefited on the basis of subjective and objective evaluation. In the remainder of the 40 per cent of the cases, the drug appeared to have no effect or produced side-effects such as extreme drowsiness, mental cloudiness, peculiar feelings of disassociation, "suddenly feeling very old". In these cases, drug discontinuance was necessary.

TABLE III
COMPARISON OF LEVEL OF MG. HCL WITH THREE MEDICATIONS

Time	Prochlorperazine- Isopropamide	Prochlorperazine	Placebo
Fasting specimen	2	4	10 (-2)
15 minutes	1	4 (-1)	12 (-2)
30 minutes	3 (-2)	4	8 (-2)
45 minutes	4 (-2)	3 (-2)	6 (-3)
60 minutes	1 (-2)	3 (-1)	8 (-2)
75 minutes	3	5	9 (-2)
90 minutes	2 (-1)	4	10
105 minutes	2	6	10
120 minutes	1	2	10
Total	19	35	83

Tabulation of the number of cases with the highest figure of mg. HCl (calculated) at a given time of administration, during fractional gastric analysis, in a comparison of the effect of prochlorperazine-isopropamide, prochlorperazine and placebo. It is apparent that there is a greater number of the placebo as against the other two, and a greater number of the prochlorperazine as against the combined form and significantly less than the placebo.

Where there was a predominantly depressed state the drug appeared to accentuate this mood function and was at times not acceptable for this reason; it was more useful where psychomotor activity was intensified and excitation present. The difficulties inherent in evaluating the effective use of tranquilizers in ambulatory individuals with anxiety states as against its dramatic usefulness in obviously psychotic states is to be emphasized.

Thiopropazate appears to have a highly potent tranquilizing effect in the patient with free-floating anxiety and an almost somnifacient effect in a definite number of patients with anxiety where depression is uppermost. Its effect in this group is, however, not uniformly predictable and appears in some cases to produce side-effects. In five of the 16 subjects studied with a single dose of 20 mg. in the experimental secretory phase, five experienced marked drowsiness the same and the following day.

Clinical effect of combined propantheline-thiopropazate:—Seventy per cent of the patients with chronic gastrointestinal problems were appreciably benefited by the use of the above combination. In this series of 22 cases the addition of the tranquilizer to the anticholinergic drug, especially in the peptic ulcer and irritable colon group, led to a noticeable enhancement of the anticholinergic action especially with respect to a general feeling of increased well being. This seemed to apply as well to the duodenal ulcer cases in whom previously propantheline alone had been used for ulcer pain relief. Here the addition of thiopropazate was followed by a feeling of things being "smoothed out" in a definite manner. It has been suggested by some observers that whatever additional improvement is achieved with tranquilizers can only be ascribed to the central effects of the drug.

In the 30 per cent who failed to respond were two cases of recurrent duodenal ulcer episodes of bleeding as part of the past history. These received no benefit preferring rather the pure anticholinergic or a belladonna derivative used by them in the past. Included in this group were three cases with the postgastrectomy syndrome whose symptoms were not appreciably affected. As in our previous experience with propantheline alone in the therapy of peptic ulcer recurrences of ulcer attack were not affected, nor did complications fail to supervene at later periods⁹.

Side-effects were present in 8 per cent of the cases and were chiefly that of drowsiness. Mydriasis was not encountered. In one patient with the irritable colon syndrome, urinary frequency occurred.

In the cases of ulcerative colitis and regional ileitis observed, the drug appeared to play only a subsidiary part in the therapeutic regimen but was at times helpful especially in the case of episodes of diarrhea and should well be included in the therapeutic regimen of these two conditions. In addition to the primary antisecretory effect of the anticholinergic the specific symptom response, when the tranquilizer was added, was described variously by a number of the patients to be that of "relaxation", "increased cheerfulness", "calms me down" and "it smoothed out my insides".

Clinical effect of sustained release prochlorperazine-isopropamide combination:—Twenty-eight cases were administered the above medication either alone or as an adjunct in an over all program of treatment specially designed for the specific problem. Seventy-five per cent of these cases were benefited when the

effect was adjudged as either excellent or good. The response of the remainder was either fair or poor. The most marked response was achieved in the group of irritable colon cases and more especially when there was a manifest agitated anxiety component present. In cases where the disturbance was characterized by deep-seated and pronounced anxiety bordering on the prepsychotic state, (two cases eventually required electroshock therapy) with severe depression, endogenous or reactive, the medication had only a minimal effect. When spastic constipation was the only outstanding symptom, there was, in the isolated case, improvement in bowel activity. Thus it was used with good effect in conjunction with bulk-producers and psyllium seed preparations in these cases.

Side-effects occurred in 5 per cent of the cases in this group consisting chiefly of drowsiness. One patient stated that after two weeks of the drug her depressed state became more intense ascribing it to the medication.

A rather interesting and fairly reproducible observation worthy of comment as a sidelight in this clinical study is that the anticholinergic drugs alone or in combination are not tolerated well by patients complaining of symptoms due to esophageal hiatus hernia with or without an associated peptic esophagitis. When administered to five out of seven cases the symptoms were clearly exacerbated. The explanation may lie in the antomotor effect of the drug, favoring the retention of acid in the herniation with greater likelihood of acid regurgitation. The symptoms in this group were more generally easily controlled by the use of neutralizing antacid substances, sedation and bland diet.

Comparison of the effectiveness of the combined forms:—The two combined drug forms under study appeared equally effective in approximately the same percentage of cases and were also comparable qualitatively. The most clear cut response occurred in the isolated cases of functional diarrhea with periodic recurrences. These patients responded equally well and effectively to either medication.

They proved alike also in their limitations in that they appeared to play a subsidiary role and as adjuncts only in the chronic gastrointestinal conditions where we have learned that a comprehensive therapeutic program is necessary. This applied to conditions such as chronic ulcerative colitis and regional ileitis.

COMMENT

The effect of specific tranquilizing agents on gastric secretion other than reserpine has been studied by a number of observers. Bodi and coworkers¹⁰ reported no observable effect of meprobamate in single doses up to 600 mg. and in multiple doses up to 400 mg. t.i.d. for one week on gastric secretory patterns or emptying time in patients with gastrointestinal disease. Bandler and Whitmore¹¹ concluded that 800 mg. meprobamate administered through a Levin tube did not have any significant effect on the concentration of free hydrochloric acid or the volume of gastric juice produced in the ulcer patients

and in a group of control patients and stated that the rationale for its use in the treatment of patients with duodenal ulcer would appear to be for its "tranquilizing properties" in those cases associated with anxiety and tension states. Haverback and coworkers² reported that chlorpromazine failed to influence gastric secretion.

Prochlorperazine in the usual doses is reported as showing no stimulating effect on gastric secretion, but in pharmacologic studies¹¹ at experimental dosage levels it is reported as producing definite inhibition of gastric secretion. Harrison and Packman¹² are quoted as stating that hydroxyzine lowers or suppresses gastric secretion.

The possibility that some tranquilizing agents in doses at the clinical or at varying markedly increased experimental levels produce suppression of gastric secretion should be considered. The evidence with reference to thio-propazate and prochlorperazine accumulated in this study on normal subjects, suggests that these two agents may have inherently suppressive influence of their own on the levels of production of hydrochloric acid. Further corroborative studies are necessary in both normal individuals and patients with duodenal ulcer and known hypersecretors.

When these are added to anticholinergics with well validated^{13,14,15} gastric secretory inhibitory and antispasmodic effects, the combination clinically appears in studies by other observers^{16,17} in the case of the isopropamide-prochlorperazine combination to provide an additional factor of increased usefulness. Our clinical experience with this prolonged acting combination as with the propantheline-thiopropazate medication provides clinical data in confirmation of these observations. The figures of good to excellent results in the range of between 75 to 85 per cent of patients in this group of gastrointestinal disturbances seems to vary little in other reports¹⁸. In placebo double-blind studies as for example with isopropamide alone¹⁹, the figures are between 40 to 50 per cent of good to excellent results for the placebo.

In the course of this experimental and clinical study the following questions have perforce arisen: Can tranquilizers, by exerting a preponderantly central effect, be of critical value alone in the treatment of gastrointestinal disease? Can we anticipate a fully adequate attack in the therapy of peptic ulcer by relying on this modality alone to the exclusion of restricted diets, anticholinergic drugs or antacids? The inestimable boon to countless ulcer sufferers of the lack of the need to adhere to a strict dietary program is obvious.

A full scale clinical study in duodenal ulcer patients, employing the double-blind method where complete liberalization of the diet has been combined with the administration of tranquilizers is in progress by our group of observers. Similar studies in small series have been studied elsewhere.

The evaluation of treatment of peptic ulcer and functional gastrointestinal disease is made difficult by the tendency for spontaneous remissions and periodic

exacerbations. Improvement under therapy may well be coincidental rather than due to cause and effect. As with observers of long experience¹⁸ reliance was placed on careful follow-ups, a history of the number of previous recurrences, the use of the patient as his own control and a comparison with similar patients treated with other comparable combinations. We were also aware of the real factor of psychotherapy, and support operating throughout the study; indeed the usefulness of the tranquilizing agents to a degree, may rest in rendering the patient more amenable and receptive to this factor in treatment.

In recent decades, attention to the psychosomatic aspects of gastrointestinal disease has coincided with the upsurge in our knowledge of the action of neuro-psychotropic drugs in the psychoses and the psychoneuroses. Attempts have been made to validate the mechanisms involved in the interrelationships between these and the psychosomatic diseases. As a group, the tranquilizers are providing us with an effective therapeutic tool with which to explore these vaguely-defined areas.

CONCLUSIONS

1. An experimental study to determine the effect of tranquilizers on gastric secretion and a long-term clinical testing of the usefulness of tranquilizers combined with anticholinergic drugs in gastrointestinal disease was carried out.
2. One hundred and four fractional gastric analyses in normals were done using the placebo method. Sixty cases of ulcer and related disturbances were treated. In this instance, thiopropazate and isopropamide were chosen.
3. Thiopropazate at experimental dosage and prochlorperazine alone and in combination with isopropamide inhibit basal gastric secretory acid when compared to a placebo.
4. Approximately 75 per cent of the cases treated clinically with tranquilizer-anticholinergic combinations using the above types were benefited appreciably when they were employed as adjunctive therapy in the over all management in these varied conditions.
5. Side-effects were present in 5 per cent of cases, consisting chiefly of drowsiness. The drugs appeared also to affect adversely symptoms associated with esophageal hiatus hernia with peptic esophagitis.
6. Thiopropazate, when administered alone, was somewhat unpredictable clinically, in cases of anxiety where depression was predominant. It, however, enhanced the effect of propantheline in the usually dispensed doses in functional gastrointestinal disease.
7. The effect of specific tranquilizers in gastrointestinal disease may be exerted by their possible inhibitory effect on gastric secretion as well as by central action.

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SUBLINGUAL AND SUPPOSITORY THERAPY IN INTERNAL MEDICINE*

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The use of sublingual tablets and rectal inserts for administration of medication is becoming of increasing importance in all fields of medicine. This is certainly a logical development, as it often enables the patient to administer his own medication rather than rely upon a physician or someone else to provide subcutaneous or intramuscular injections. Many clinical entities are accompanied by such profound nausea and vomiting that all medication is promptly rejected, or inadequately absorbed. Even the thought of taking medication by mouth makes many of these patients worse. Sublingual and rectal absorption is usually much more rapid than that from the upper gastrointestinal tract (Figs. 1 and 2).

This rapid absorption is often of considerable importance in quickly allaying symptoms of bronchial asthma, migraine headaches, angina pectoris and other medical conditions. Tables I and II present some of the more common conditions treated and medications used by the sublingual and rectal routes.

Local conditions in the mouth do not appreciably interfere with absorption by the sublingual route. This, however, is not the case with the rectum. It is only too evident that maintenance of the anorectal structures in good condition is of the utmost importance. The nerve supply to this area and the symbolic significance that is often consciously or unconsciously associated with the rectum makes this region a very sensitive area. These factors provide the proctologist with the ever-increasing challenge to handle these tissues with utmost care and gentleness whenever he is called upon to treat them either medically or surgically. This forethought on the part of the proctologist will enable the medical man to use the rectum for administration of medication in the future care of these patients, whereas whenever local irritations, diseases or therapy to this area leave excessive scar and irritation, the rectal route of administration of therapy is lost to the patient.

PHYSIOLOGY OF SUBLINGUAL ABSORPTION

"Gastric and upper intestinal juices and the liver often destroy or inactivate medication taken by mouth. When the tablet is placed under the tongue, or

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in the buccal pouch, properly prepared medication is absorbed directly into the systemic circulation by way of the sublingual or buccal blood vessels and lymphatics, thus by-passing the liver¹. The advantages of sublingual therapy has been aptly expressed by Goldberg, by three "Ees": Ease of administration, Efficiency and Economy. The patients find sublingual tablets to be pleasanter and more convenient than injections. They often are more effective than tablets which are swallowed, and, at times, almost as effective as injections (dose for

TABLE I
SUBLINGUAL MEDICATIONS IN CURRENT USE

<i>Condition Treated</i>	<i>Medication administered</i>
1. Bronchial asthma	Isoproterenol hydrochloride
2. Angina pectoris	nitroglycerine pentaerythritol tetranitrate
3. Weight gain	methyltestosterone and its newer related analogs
4. Sexual retardation in adolescent boys	methyltestosterone
5. Male hypogonadism	testosterone compounds
6. Addison's disease	desoxycorticone acetate
7. Gynecological conditions	progestational substances
a. control of bleeding in <i>metropathia hemorrhagica</i> (menometrorrhagia)	
b. production of withdrawal menses in estrine primed endometrium	
c. Threatened or habitual abortion	
8. Localized infections	proteases: streptokinase and streptodornase
Allergies	
Surgery	
Dentistry	
9. Hyperlipemia	anticoagulants heparin
10. Migraine and other types of vascular headache	rapidly soluble ergotamine tartrate tablets

dose). They are more economical and more convenient than repeated injections (see Fig. 1).

PHYSIOLOGY OF RECTAL MEDICATION

Before one resorts to rectal administration it is a good rule to make a digital examination of the rectum. In this manner, excessive irritability that would require unusual care to secure retention of the medicament can usually

be detected; or, when the rectum is filled with feces and the patient has no desire to defecate, rectal stasis may be diagnosed and a rather insensitive rectum may be assumed to exist. A rectum distended with fecal matter should be cleaned out by an evacuant enema before it is given the task of receiving medication. Sometimes anal fissure, inflamed hemorrhoids or cancer make rectal administration so painful as to be inexpedient unless demanded by the condition itself².

The dose by rectum was formerly assumed to be double that by the stomach, but it is probably more nearly correct to consider it one-half the oral dose, at least for certain substances. Actual experiments have shown that phenol as well as alkaloids, such as strychnine, morphine, atropine and epinephrine, are more toxic when given by rectum than when administered by mouth. This is explained partly by the fact that the stomach has poor absorptive quality and partly by the circumvention of the destructive action of the liver on these substances, some of the absorption being carried on through the inferior hemorrhoidal veins, which empty directly into the inferior vena cava.

In 1950, Truit, McKusick and Krantz³ made a comparison of the theophylline blood levels after oral, rectal and intravenous administration. It was then fully appreciated that very satisfactory blood levels could be obtained by the rectal administration. Waxler and Schack⁴ reporting in the *Journal of the American Medical Association* on the administration of aminophylline in 1950, made a comparison of the intravenous, intramuscular, oral and rectal routes.

Suppositories, which are solids conveniently shaped for insertion into the rectum, require no apparatus. Hence, they may be considered the preferable form of rectal administration, unless special reasons render other forms desirable.

Many excellent studies have been conducted recently on the physiology of suppository administration of various medications⁵⁻¹¹.

SPECIFIC CONDITIONS TREATED BY SUBLINGUAL MEDICATION

1. *Asthma*, being one of the acute medical emergencies seen so commonly in general medical practice, naturally has been subjected to every conceivable treatment administered by every possible route and by all kinds of apparatus and gadgets. Hypodermic injection of adrenalin is still the most rapid and most efficacious treatment for the average acute attack. Many patients can obtain essentially the same relief by sublingual administration of isoproterenol hydrochloride as by adrenalin. Average adult dose, 1 Glosset (sublingual tablet) of 15 mg. In some cases 1 Glosset of 10 mg. suffices; in other cases 2 Glossets of 10 mg. are required. For children, 5 to 10 mg. ($\frac{1}{2}$ to 1 Glosset of 10 mg.). A total of 60 mg. in one day should not be exceeded (15 mg. four times daily or 20 mg. three times daily).

2. *Angina pectoris*:—The mainstay of treatment for angina pectoris has always been sublingual tablets of nitroglycerine. The dosage of this has to be individualized for each patient. Once this is determined, the patient soon learns to insert one tablet (usually 1/100 grain or 1/200 grain per tablet) under the tongue at the onset of any chest pain or discomfort. When relief is obtained, it is safe to repeat this as often as necessary throughout the day. Newer tablets have been recently marketed, including nitroglycerine and pentaerythritol tetranitrate. The purpose of this is to have the nitroglycerine exert an immediate effect and to have the pentaerythritol tetranitrate maintain a longer-acting vasodilation of the coronary arteries.

3. *Weight gain*:—It has long been known that testosterone stimulates the formation of body tissue in general and prevents tissue loss in various wasting diseases. As Fuller Albright so aptly put it, "one has only to compare the physique of a bull with that of a steer"¹². Androgens favor the conversion of dietary nitrogen into protein. In addition, potassium phosphorus and sulphur are retained in about the same ratio with nitrogen as they are found in protoplasm, and weight thus gained is in protein tissue, not in fat or edema. Because of the fact that androgens favor utilization, but do not manufacture protein or other elements of protoplasm, the intake of calories, protein and carbohydrate must be adequate. The nonspecific protein building effects of methyltestosterone can be beneficial in many different debilitating diseases and in surgical convalescence. The sublingual dose for females varies between 5 and 10 mg. per day, and for males 10 to 40 mg. daily. It is desirable in women to use the smallest dose which will produce weight gain without masculinization of excessive libido¹³.

Specific improvement as well as weight gain and other anabolic effects has been provided by sublingual methyltestosterone in inoperable breast cancer, postmenopausal osteoporosis, Cushing's syndrome and hypophyseal cachexia or Simmond's disease¹³.

4. *Sexual retardation in adolescent boys*:—Abnormally short, slender boys with sexual retardation, whose bone age is less than chronologic age, respond well to sublingual methyltestosterone, on a dose of 5 to 20 mg. daily. With improved physical development, the boys lose their feeling of inferiority and embarrassment, become more cooperative, mature, concentrate better in school, and are accepted by groups of their own age. The only complications are gynecomastia and tender nipples, which demand interruption of treatment¹⁴.

5. *Male hypogonadism*:—While androgen therapy is convenient, inexpensive and usually effective in hypogonadism to primary testicular failure or to testicular failure secondary to hypofunction of the pituitary gland, hypogonadism present prior to puberty, during puberty or after puberty all seem to respond quite satisfactorily in most instances. Although initial high dosage

may have to be given, maintenance doses of 5 to 20 mg. daily often has a stimulating rather than a depressing effect on the testicles¹⁵.

6. *Addison's disease*:—Prior to the advent of cortisone, desoxycorticosterone acetate, the mainstay of treatment of chronic Addison's disease, daily intramuscular injection, or infrequent pellet implantations were at first considered mandatory. In 1942, Thorn, Dorrance and Day¹⁶ found that the average intramuscular dose was 3.8 mg. when 3 to 4 gm. of salt was supplemented. Hard compressed sublingual tablets, each containing 2 mg. administered morning and night, readily maintains the average Addisonian patient. More direct

TABLE II
MEDICAL TREATMENT BY RECTAL SUPPOSITORIES

<i>Condition Treated</i>	<i>Medication Administered</i>
1. Bronchial asthma	Theophylline-Ethylenediamine
2. Migraine headache	Ergot-caffeine combination suppositories with or without sedatives, antispasmodics, tranquilizers and antihistaminics
3. Nausea and vomiting accompanying acute gastroenteritis	Sedative-antispasmodic combinations, Phenothiazines
4. Nausea and vomiting accompanying upper respiratory and influenzal infections	Sedative-antispasmodic combinations, Phenothiazines
5. Dysphagia associated with neurologic conditions	Sedatives, tranquilizers, Phenothiazines
6. Dysphagia associated with hysteria, menopause	Sedatives, tranquilizers, Phenothiazines
7. Insomnia or anxiety, accompanied by dysphasia or nausea	Sedation
8. Rapid relief from pain associated with gastrointestinal disturbances	Sedation, analgesia or even narcotics

measures, however, are necessary during crises or under circumstances that could possibly lead to crises¹⁷.

7. *Gynecologic conditions*:—When basal body temperature charts show an absence of cyclic activity, there usually is lack of ovulation, therefore lack of progestational activity. When this is present in a case of menometrorrhagia, sublingual administration of 10 mg. tablets of progesterone b.i.d. beginning the twelfth to the fourteenth day in the menstrual cycle will often control the bleeding. This same dosage will help to bring about withdrawal menstruation in cases of amenorrhea that have been previously primed with estrogen. Patients with regular menstrual periods, complaining of premenstrual tension and mastodynia with absence of cyclic basal temperature activity will usually respond

to 10 to 20 mg. of progesterone administered daily. In some cases, this is needed for the entire two weeks prior to menstruation, whereas in others a good response is obtained from therapy for five to seven days before onset of menstruation.

Threatened abortion is treated with 40 to 60 mg. of progestational substance daily until one week after cessation of pain and hemorrhage. The woman should then be maintained on 20 to 40 mg. daily until delivery.

In habitual abortion, sublingual therapy with 20 to 30 mg. daily should be started with the diagnosis of pregnancy and continued to the seventh month¹⁸.

8. *Localized infections*:—The edema that usually accompanies inflammation and the fibrosis that often follows can hinder recovery by causing dysfunction and deformity. Certain proteases are available for use in redissolving fibrin deposits, reducing edema, and otherwise keeping the inflammatory responses of the body within bounds. The rational use of proteases for this purpose depends on an accurate appraisal of the existing disease in terms of the particular stage, duration, intensity and degree of localization of the inflammatory process at the moment. Trypsin, streptodornase, and streptokinase are active when given by either buccal or the parenteral route. They are effective when given by mouth in many situations, especially in certain localized infections and allergies, in surgery and in dentistry. Individual tablets, or tablets containing combinations of the various proteases are available containing 10,000 or 20,000 units per tablet. The average dose is 10 to 20 thousand units, sublingually, q.i.d.

9. *Hyperlemia*:—Clearing of alimentary lipemia after injection of heparin was reported by Hahn in 1943¹⁹. Engelberg, Kuhn and Steinman²⁰ demonstrated in 1956 that injections reduced the anticipated mortality of elderly patients with severe coronary atherosclerosis. Litwins et al²¹ reported successful absorption of heparin administered sublingually in 1951. Subsequent reports^{22,23} could not confirm the efficacy of sublingual administration of heparin. Engelberg²⁴ found sublingually administered heparin potassium tablets ineffective in 85 per cent (18 of 21) of patients, and recommended that parenterally given heparin should be used when this type of therapy is indicated.

10. *Migraine and other types of vascular headache*:—In our extensive experience with diagnosis and treatment of headache, therapy with sedatives, analgesics, antispasmodics and ergot derivatives of various forms and combinations has proven to be the mainstay of symptomatic therapy. Many patients with anxiety-tension states have tension headaches on an emotional, psychic or muscular tension basis. Many patients with vascular type headache experience pain when vasodilation of branches of the external carotid artery occurs. The classical type of this vasodilating headache is migraine. Other forms seen with less frequency are histaminic cephalalgia, hypertensive headache and temporal

arteritis. In addition to this, there are often vascular features to the above-described tension headaches. One of the cardinal symptoms of these vascular headaches is nausea, often followed by severe retching and vomiting. Before development of suitable sublingual tablets and rectal suppositories²⁵⁻³⁴ it was necessary to instruct the patient or a relative in the technic of administering medication by hypodermic injections. As could be expected, this was often impossible to perform, thus requiring the physician to make repeated home visits to these patients, merely to administer sedatives or ergot derivatives by hypodermic injection. Since 1942, we have taken part in the development of,



Fig. 1—Physiology of sublingual absorption. When the tablet is placed under the tongue or in buccal pouch, the medication is absorbed directly into the systemic circulation by way of the sublingual or buccal blood vessels and lymphatics, thus by-passing the liver.

and have tested many different ergot derivatives alone and in combination with caffeine, sedatives, antispasmodics, antihistaminics, analgesics and tranquilizers. In an effort to afford the patient the benefits of rapidly acting ergotamine tartrate, administered in a pleasant, esthetically acceptable manner, we have tested several forms of sublingual tablets. Among these is a saliva-soluble tablet, containing 2 mg. of ergotamine tartrate. This has been thoroughly evaluated in a series of 52 patients with various forms of vascular headache. Table III records the different types of headache treated and the results with the

new tablet and with formerly used ergot preparations. It will be seen that 83 per cent of the migraine and related types of tension-vascular headache patients reported a satisfactory result, and 13 per cent did not respond. This compares with the effect of previously used medication. Many tension headaches have predominant anxiety, emotional or other psychosomatic problems, associated with the headache, and the addition of sedatives, analgesics and tranquilizers to ergot and caffeine would be expected to produce a better result in these patients than ergot alone. Cranial arteritis and patients with symbolic type of

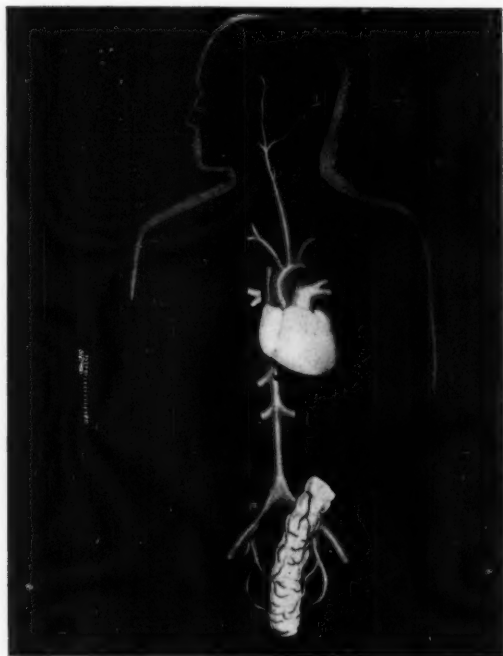


Fig. 2—Physiology of absorption from lower gastrointestinal tract. This drawing shows that the venous return from anorectal area enters the inferior vena cava directly from the lower hemorrhoidal veins, and thus by-passes the liver. Absorption from the upper gastrointestinal tract, on the other hand, must enter the portal circulation, and thus travel through the liver before entering the major circulation.

headache, associated with actual psychosis (depressions) were not expected to respond to ergot therapy, and did not respond to the sublingual tablets or to other ergot therapy. The fact that 4 patients with histaminic cephalalgia reported a satisfactory response to sublingual ergot, whereas none reported response to other ergot combinations was also understandable. The 7 patients included in this group had typical histaminic cephalalgia, each attack lasting less than a period of 40 minutes. It is rare for a patient to be able to receive

an intravenous injection of dihydroergotamine immediately at the onset of a histaminic cephalalgia attack. Unless the ergot is able to get into the blood stream immediately, such as by intravenous injection or rapid sublingual absorption, it cannot be expected to abort the attack in less than one-half hour.

As a result of this study, it is our opinion that sublingually administered ergotamine tartrate is effective in a large proportion of migraine and other vasodilating type of headache attacks.

SPECIFIC CONDITIONS TREATED BY RECTAL MEDICATION

1. *Constipation*:—Retention of rectal feces content often takes place because of irritation in and about the anus. The patient tries to avoid irritation and pain in this area by not moving the bowels. Correction of these irritated

TABLE III
RESPONSE TO SUBLINGUAL ERGOTAMINE TARTRATE

Diagnosis	No. Patients	Response			Side-effects		
		Excellent	Good	Poor	Nausea	Lassitude	None
Migraine and related tension-vascular type headache	41	29	5	7	10*	7*	
Cranial arteritis	1	0	0	1			1
Psychogenic	3	0	0	3			
Histaminic-cephalgia	7	3	1	3	1*		

*These occurred in 13 patients, 5 reported more than one side-effect.

areas is the first step in alleviation of this type of constipation. Constipation also can occur on a physical basis, due to relaxation of the perineal tissues following surgery or childbirth. In these instances, it is often necessary to the patient to physically start the bowel movement by means of suppositories or enemas. While the best therapy for such conditions is surgical repair to these relaxed tissues, this is not always feasible. For this reason, maintenance of proper tissue continuity and repair of any local lesions is imperative.

2. *Relief of pain*:—Painful areas in and about the rectum have long been treated by application of salves or analgesic suppositories for their local action. In addition to this, there is a much larger field for analgesia to be administered by rectal route. I have long made a practice to prescribe suppositories consisting of $\frac{1}{4}$ or $\frac{1}{2}$ gr. belladonna and 1 gr. of opium powdered extract to adults for acute painful conditions. These have included severe cardiac pain, unresponsive to

nitroglycerine, pain following trauma, sprains or fractures, severe abdominal crises of various forms, such as occurs in ulcerative colitis, hyperirritable spastic bowel conditions, gallbladder and renal colic, and in severe incapacitating headaches, unresponsive to routine ergot therapy.

It might be wise here to add an explanatory note and also a word of caution. As with administration of narcotics in any other form, their use by means of rectal suppositories should not be given over a long period of time or frequently for recurrent conditions. They are, however, often of great benefit for emergency situations that occur infrequently. My experience with the treatment of headache has been quite extensive. There are patients in whom severe attacks occur at very infrequent intervals, and do not respond to non-narcotic medication. Occasional use of the opium suppositories in these instances is indicated under proper supervision.

3. *Asthma*:—One of the mainstays for treatment of acute asthmatic attacks has long been theophylline-ethylamine-diamine. Its slow intravenous administration often provides dramatic relief in *status asthmaticus*, as first introduced by Dr. George Herrmann of Texas. Although many forms of oral theophylline derivatives are prescribed repeatedly for these cases, in my experience this route of administration has not been of sufficient benefit to make it worthwhile. In addition, when large doses are given orally, nausea and other gastrointestinal disturbances are produced in a high percentage of cases. I have found that the use of aminophylline suppositories, gr. 7.5, every eight to 12 hours provides lasting and prolonged relief in many cases of bronchial asthma. To the best of my knowledge, Dr. Alvin L. Barach of New York City was the first to call attention to the excellent therapeutic response from the rectal installation of aminophylline in intractable asthma³⁵. This principle has been recently adapted to the use of another theophylline derivative, theophylline-mono-ethanolamine (Clysmathane, Fleet), which is available in a disposable rectal plastic unit containing 37 c.c. Some patients find this to be more easily administered and more esthetically acceptable. With the proper use of this unit, it is unnecessary for the fingers to touch the anal parts. This solution is introduced just inside the internal anal sphincter so that most of the solution will reach the inferior vena cava by way of the inferior hemorrhoidal veins and thus by-pass the liver. This is deemed to be a decided advantage as it is felt that therapeutically it is much better to have the theophylline solution reach the systemic circulation without going through the liver as a certain percentage of the theophylline must be metabolized in that organ³⁶.

Although untoward reactions to aminophylline administered in this manner are few and far between, they do occur. Therefore extreme caution should be taken with the use of this drug in any form^{37,38}.

4. *Headache*:—Since 1946 we have taken part in the development of many forms of rectal suppositories for the treatment of headache. From Table IV it

is seen that the most complete preparation now available is Cafergot PB suppository. This contains Pentobarbital Sodium, 60 mg., Bellafoline, 0.25 mg., Caffeine, 100 mg., Ergotamine tartrate, 2 mg., which gives a balanced formula to therapy of such conditions. The ergot and caffeine act synergistically as vasoconstrictors on the dilated cerebral arteries. The bellafoline helps to relax gastrointestinal irritability, which accompanies the attack or might be aggravated by the ergot. The pentobarbital sodium is of great benefit in allaying the apprehension and anxiety associated with the headache episodes. As seen by

TABLE IV

ERGOT THERAPY FOR VASCULAR HEADACHE AND THE VASCULAR COMPONENT OF TENSION HEADACHE

Medication	Method of Administration	Initial Dose	Subsequent Dose
(Administered by Physician) Dihydroergotamine Ergotamine tartrate Dihydroergotamine	Intravenous Intramuscular Subcutaneous	1 c.c.-1 mg. $\frac{1}{2}$ c.c.-.25 mg. 1 c.c.-1 mg.	Not needed Not needed 1 c.c. in one hour?
(Administered by Patient) Ergot-caffeine combination suppositories	Rectal	1 suppository	1 suppository in one hour seldom needed
Ergot-caffeine suppositories	Rectal	1 suppository	1 suppository in one hour as needed
Ergot-caffeine combination tablets	Oral	2 tablets	1 every half hour till relief or total of six
Ergot-caffeine tablets	Oral	2 tablets	1 every half hour till relief or total of six
Sublingual ergotamine tartrate	Sublingually	1 tablet-2 mg.	Repeat in 10-15 minutes if needed
Rectal dispenser (delivers 1 c.c. of fluid containing ergotamine tartrate, 2 mg. Caffeine USP 100 mg.)	Rectal insertion	$\frac{1}{2}$ to 1 c.c.	Repeat in 15-30 minutes if needed

the chart, the suppositories are to be administered at the onset of such attacks, and can be repeated in one to two hours, if necessary. Although we have many patients that have taken one or two suppositories daily for years³⁹ it is a good plan to limit the total intake of ergot for any one patient to 10 to 12 mg. of ergotamine tartrate per week. Although there have been occasional reports of ergot toxicity after its use by injection, to my knowledge there have been no severe untoward reactions to its oral or rectal use, if administered under adequate medical supervision.

Another recent innovation is the Rectalad dispenser, which is a small disposable plastic syringe. Each of these contains and delivers 1 c.c. of a stable concentrated solution of ergotamine tartrate, 2 mg., caffeine, USP 100 mg., in a suitable solvent with slight local anesthetic properties. This rectal formulation has proven particularly useful in the early treatment of migraine or other vascular headache attacks, as it permits prompt absorption with very rapid establishment of therapeutic plasma levels. It is packaged in such a way that it can be carried in the pocket or purse, and is not affected by extremes of temperature, as suppositories often are. This makes it most convenient for patients while traveling or away from the office or home at any time.

In addition to the above-described symptomatic therapy with ergot suppositories, frequently recurring nocturnal attacks can often be prevented by insertion of one Cafergot PB suppository at bedtime. This enables the patient to get necessary rest and sleep, which is helpful in breaking up cycles of headache. This has been found true, even in hypertensive and cardiac patients, in which the improved relaxation, freedom from headache attacks, and uninterrupted sleep has actually helped to bring about an improvement in their cardiac condition. The suppositories seem to have a more rapid and stronger effect than the tablets, which may be due to direct absorption into the systemic circulation and avoidance of the immediate detoxication by the liver.

In addition to these specific entities described, any other medical condition associated with nausea and vomiting might benefit from adjunctive therapy with sedatives, antispasmodics, antihistamines or some of the newer ataractics or tranquilizers, which have been quite effective in allaying nausea and vomiting. Once this is allayed, oral medication with analgesics, antibiotics, antacids, etc., can be resumed.

SUMMARY

It has been a pleasure to discuss the use of the sublingual and the ano-rectal portals of administration of medication for internal medical conditions. Once the patient has been taught the proper technic of administration of his drugs for his specific medical condition, and has found that he indeed obtains satisfactory results in this manner, his confidence is markedly increased. He now realizes that he does have means at hand to alleviate his attacks whenever they occur, and does not live in continual fear and anxiety that he will be overwhelmed, and have to call frantically for his physician. In turn, the physician also received an added benefit for not being called away from his office or awakened in the middle of the night to care for these medical emergencies that can be handled so readily by sublingual or rectal medication.

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MALIGNANT DEGENERATION IN CHRONIC INFLAMMATORY DISEASE OF THE COLON AND SMALL INTESTINE*

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and

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Malignant degeneration as a complication of chronic ulceration of the colon due to ulcerative colitis has long attracted the attention of many authors and reports from many of the large hospitals and clinics have been published. The incidence of cancer of the colon has varied widely in these reported series. In 1949 Kasich, Weingarten and Brown¹ reported the occurrence of malignant degeneration in ulcerative colitis in 149 cases studied at Montefiore Hospital in New York. Seven cases and an incidence of 4.9 per cent with highly malignant growth and early metastases were presented.

In an editorial shortly after this, Alvarez² called attention to the chief points of interest in such cases: as the youth of the patient, the tendency to multiple cancers in the colon, and the "wild fire spread" type of cancer which arises in the ulcerated colon.

Now in 1959, close to 600 cases of chronic ulcerative colitis have been reviewed and studied at Montefiore Hospital. The incidence of cancer has somewhat increased, being close to 6.5 per cent of all cases.

In the literature there seems to be considerable variation in the frequency of this complication as it was observed by different authors. There are different reasons for these figures, such as the failure of follow-up, duration of disease, early colectomies, etc. Our conclusions are the same as many authors, that cancers of the colon and rectum are found to be many times (about 5-6 times) more prevalent in cases of ulcerative colitis in comparable age groups of the general population. The predisposition to cancer of the colon in younger age groups in chronic ulcerative colitis of long-standing (over five years) is particularly striking. The common occurrence of malignancy in defunctionalized colons is again mentioned as it emphasizes the necessity of more radical therapy.

PATHOLOGICAL CONSIDERATIONS

We still agree with the statement that the cause of malignant degeneration in ulcerative colitis is unknown. Pathologists and cancer research groups, how-

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ever, have long accepted the theory of tumor genesis in chronic irritation and inflammation.

Remissions and exacerbations are common in chronic ulcerative colitis. Repair and formation of new tissue are noticed in the areas of healing. In Bargen's cases, pseudoadenomatous polyps develop in 10 per cent of cases of chronic ulcerative colitis³. Our percentage has been somewhat higher . . . about 15 per cent. We feel as others do today that there is a definite trend first to the formation of adenoma and thence to carcinoma.

While no definite statement on this subject can be made, we, as most observers, favor the theory that carcinoma of the colon in ulcerative colitis arises



Fig. 1a



Fig. 1b

from adenomatous polyps and that these in turn develop from pseudopolyps. These are not truly pseudopolyps, but rather isolated islands or nests of mucosal tissue remaining in a denuded and eroded colon that have become inflamed and edematous and appear to be protruding into the lumen simulating polyps.

Visualization of lesions by sigmoidoscopy or x-ray studies establish the diagnosis. There is, no doubt, more alertness to carcinoma in ulcerative colitis now than in previous years. Patients who are not treated surgically should be under constant surveillance and change in symptoms, excessive weight loss, anemia, bleeding, etc., should remind us of the possibility of carcinoma in ulcerative colitis. This is particularly important in patients who are on steroid

therapy. Proctosigmoidoscopy and x-ray examination should be done to determine the presence of polyps. Finally, it should be borne in mind that total colectomy, if more frequently performed under proper indications, might spare many young patients with ulcerative colitis.

Inflammatory disease of the small bowel, regional ileitis or nonspecific granulomatous enteritis as a disease entity, has been well known since 1769 and was first described by Crohn, Ginsburg and Oppenheimer in 1932⁴. The incidence of malignancy in the small bowel in nonspecific granulomatous enteritis

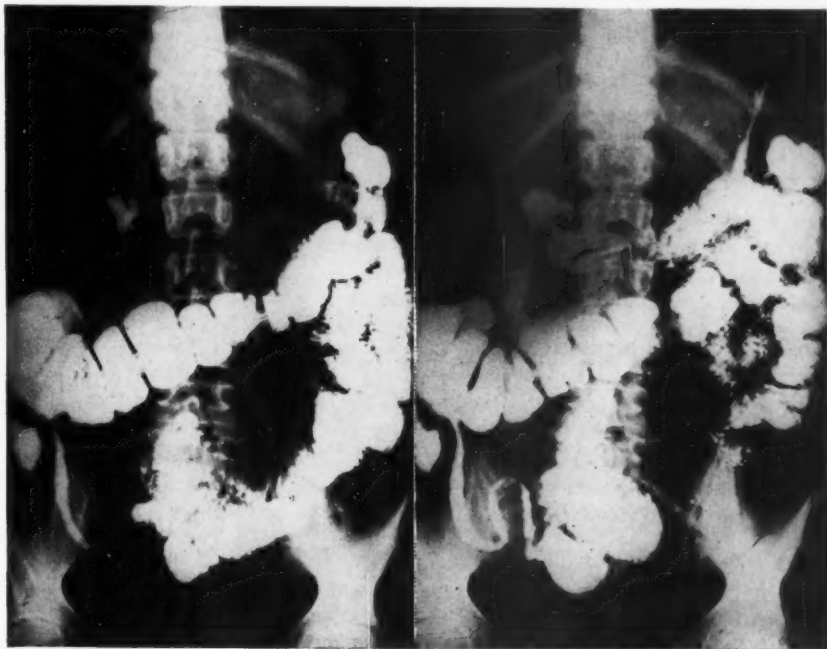


Fig. 2a

Fig. 2b

is extremely low⁵. The occurrence of adenocarcinoma in a case of long-standing nonspecific enteritis suggests the possibility of a relationship between the two entities, possibly based on the same kinds of chronic irritative phenomena that are seen in the development of carcinoma in chronic ulcerative colitis.

Van Patter and his group reported colonic involvement in regional enteritis, which occurred in their series in 37 per cent of all patients, was associated with malignant change in the colon in only 1 case out of 600⁶. Marshak and Wolf in 1955 stated that in regional enteritis "an uncommon but striking finding is the

presence of large, inflammatory polyps. . . . Carcinomatous transformation of these polyps has not been observed". The clinical follow-up and studies of this disease, however, have not been as complete as those in chronic ulcerative colitis because the chronicity of this disease permits the patient to continue ambulatory treatment and not too many die from the disease itself.

The first case of malignancy in regional enteritis was that of Ginsburg et al⁷, in 1956, with an adenocarcinoma seen in the jejunum with multiple metastases to the liver. The inflammatory disease in the small bowel appeared to have been present for 15 years and by actual roentgenographic demonstration for 4 years, before the appearance of an adenocarcinoma in the jejunum.

The second case was that by Kornfeld, Ginzburg and Adlersberg in 1957⁸, again with adenocarcinoma seen in the jejunum in a case of nonspecific granulomatous jejunitis. At surgery, adenocarcinoma of jejunum was found. Radical resection was not possible and the patient died five months after operation with wide-spread metastases.

A third case reported by Bersack, Howe and Rahak⁹ was concerned with a 26-year old patient with granulomatous enteritis for 9 years, who developed adenocarcinoma of jejunum, ileum and colon.

A fourth reported case at Montefiore Hospital¹⁰, was a 44-year old white woman who had repeated admissions to the hospital for extensive regional enteritis with strictures and jejunojejunostomy (Figs. 1a and 1b). At final surgical exploration and resection of the jejunal loop, the gross specimen showed bypassed jejunal loops studded with tumor nodules on the mucosal surface. The final pathological diagnosis at autopsy included regional enteritis involving the jejunum and ileum and adenocarcinoma of the jejunum arising in the bypassed loops. There were also metastases to regional lymph nodes, liver, lungs, etc.

Another case involved a 28-year old female with a history of recurrent regional enteritis which in the space of 5 years required surgery 3 times because of persistent stricture formation. Twenty-six months following the second operation, the patient developed a series of spontaneous fecal fistulas communicating with the outside from a section of the involved enteritis. Thereafter, her condition deteriorated rapidly and at the third operation a section of the small bowel was found to be extremely thickened, with tumor nodules scattered through the abdomen (Figs. 2a and 2b). Pathological examination revealed chronic inflammatory disease with multiple strictures and a superimposed adenocarcinoma involving all the layers except the serosa.

COMMENT

In these five authenticated cases of adenocarcinoma occurring in instances of long-standing, chronic granulomatous enteritis, the disease had been present

for a number of years before the advent of adenocarcinoma. There was no preoperative roentgen or clinic diagnosis of adenocarcinoma in these cases. The roentgen findings ordinarily associated with neoplasm were not detected in advance. In the presence of long-standing inflammatory disease, such changes may be very difficult to delineate and appreciate since they may be present during the course of inflammatory process. Zones of narrowing with proximal obstruction are found in inflammatory process without carcinoma being present. The roentgen and clinical diagnosis of a complicating adenocarcinoma in this disease entity is therefore difficult.

Dr. Crohn, commenting on our observation of the occurrence of carcinoma in a bypassed segment of chronically inflamed jejunum and ileum, called it a new observation and was pleased that we had documented it. With modern medical therapy, including steroids, antibiotics, transfusions, etc., increasing numbers of patients with chronic granulomatous enteritis with increasing longevity are to be expected. The problem of doing a bypass operation and leaving intact in the abdomen a segment of chronic inflammatory disease as against the alternative of resecting the entire diseased bowel area, must now be considered.

We hope that with this presentation, the gastroenterologist, radiologist and surgeon will be alerted to the possibility of the occurrence of malignant degeneration in long-standing chronic inflammatory disease of the large and small bowel and will consider the potential complication in evaluating therapy.

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PEPTIC ULCER: TREATMENT WITH ANTACIDS AND A MUCIN-LIKE SUBSTANCE*

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TREATMENT

Antacid therapy remains the cornerstone of treatment for peptic ulcer and hyperacidity. While a bland diet is helpful, it is difficult to obtain a good, prompt result without the application of other measures. Anticholinergics may be useful at the beginning of treatment, but their action as a form of "chemical vagotomy" may have some of the shortcomings of surgical vagotomy. The statement that "ulceration may recur while the physiologic effects of vagotomy persist"¹ applies with similar force to anticholinergic therapy. Recurrences or persistence of ulcer during the course of anticholinergic therapy have been reported by a number of investigators^{2,3}. The occurrence of systemic side-effects, as well as obstruction, hemorrhage and ulcer perforation has been discussed by Ross et al⁴. The authors suggest, in addition, that "the increase in gastric retention caused by anticholinergic drugs may prolong the gastric phase of gastric secretion".

One of the important problems of antacid therapy has always been that of obtaining prolonged, effective relief of pain. The well-known acid rebound of bicarbonate of soda, with its short duration of effect, has caused it to be discarded for long-term use. Aluminum hydroxide, magnesium trisilicate and magnesium hydroxide have not worked ideally. Relief of pain may last for only 1 or 2 hours; in many severe cases, sharp pain recurs at the 2-hour interval.

During recent years, increasing attention has been directed to the mucin coating of the stomach as a factor in resistance to ulceration and in the healing process. The basic researches of Hollander⁵ demonstrated the role of the mucus barrier of the gastroduodenal mucosa in prevention of, and recovery from, ulceration. Zaidi and Mukerji⁶ have shown that when mucin production was stimulated by administration of capicum, the experimental animal (guinea pig) was enabled to resist ulceration produced in control animals by massive doses of histamine. The greater the amount of mucus produced, the greater was the protection against ulceration.

These findings suggest that mucin or mucin-like substances may enhance the effectiveness of antacid medication. It also appears that the incorporation of such a substance may prolong the effectiveness of antacid medication.

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A study was undertaken to determine the effectiveness of an antacid combination incorporating a synthetic mucoid substance*. For purposes of clinical comparison, the same antacid combination but without the mucoid component was used in a control series of patients.

PLAN OF STUDY

Experimental:—Preliminary tests using the Shay⁷ rat technic, demonstrated the action of Balvis in preventing ulcer formation. Of the animals treated with Balvis, only 22 per cent contracted ulcers, as compared with an incidence of 73 per cent in the control animals which did not receive the antacid-mucin combination. Figures 1a and 1b show a typical protective response to the medication; Figures 2a and 2b show typical ulceration in an unprotected animal.

Clinical:—Seventy-eight patients with duodenal ulcer, gastric ulcer, and hyperacidity due to hypertrophic gastritis were chosen from the Gastroentero-

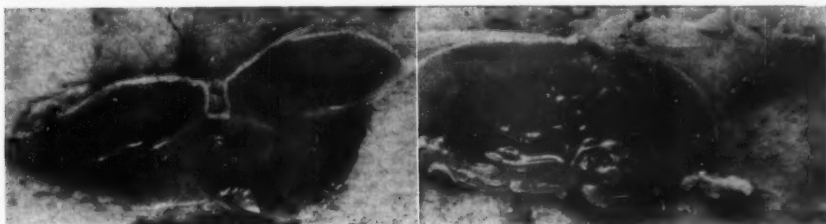


Fig. 1a

Fig. 1b

Figs. 1a and 1b—Mucosa, treated Shay rat.

logical Clinic of the Jersey City Medical Center, and from private practice. All patients had at least one gastrointestinal series of x-rays, and many had had more than one. After the diagnoses were made, the patients were placed on an ulcer diet. Eleven of the patients received 2 tablets of the combined medication every 2 hours and also received anticholinergic medication for 2 weeks because of the severity of their symptoms; in 3 of these cases anticholinergic therapy was continued for an additional 2 weeks.

Of the remaining 67 cases, 36 were given 2 tablets of the control medication (antacids without the guar cellupectinoid) every 2 hours, while the rest were given 2 tablets of the antacid-guar cellupectinoid combination every 2 hours.

RESULTS

Of the 36 patients on control medication, 26 reported improvement but all reported return of sharp pain within 1 to 2 hours; 10 were not adequately re-

*Balvis tablets, supplied by G. W. Carnrick Company, Newark, N. J., contain in each tablet: guar cellupectinoid (plant mucin complex) 275 mg.; magnesium oxide 70 mg.; aluminum hydroxide 80 mg.; and magnesium trisilicate 160 mg.

lieved of symptoms. After an interval on this control medication all 36 were placed on the antacid-guar cellupectinoid preparation. Thereafter, 33 of the patients (or 92.5 per cent) reported adequate and prolonged relief and control of symptoms. With the inclusion of these cases, all 78 patients in the study were treated with the antacid-guar cellupectinoid combination.

The results of combined therapy demonstrate the high rate of favorable responses to treatment. Table I summarizes the responses of the patients.

Patients were considered to have obtained excellent results when they experienced adequate, sustained relief; and fair results when pain recurred occasionally. Seven cases were classed as failures and had to be switched to other therapeutic measures.

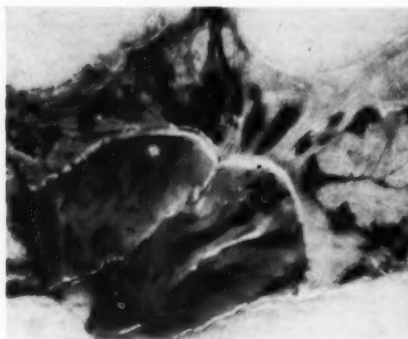


Fig. 2a

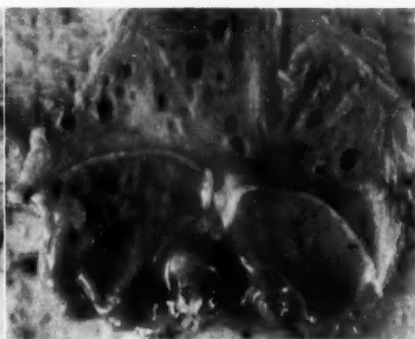


Fig. 2b

Figs. 2a and 2b—Typical ulceration in Shay rat, untreated.

Repeat x-rays, taken in several of the duodenal ulcer cases, often showed scarred duodenal bulbs. In all of the gastric ulcer cases there was complete healing where therapy with Balvis was continued.

Gastroscopic studies were done in 4 cases to determine the length of time the test medication (Balvis) and the control medication (Balvis minus the guar-cellupectinoid component) remained in the stomach. Two tablets of the control preparation were given four hours before instrumentation. Of the 4 cases, only 1 showed a small amount of medication in the stomach at the end of four hours. The same patients were similarly examined four hours after receiving 2 tablets of the test preparation. In 3 of the 4 cases there was considerable evidence of medication adhering to the gastric mucosa.

The intriguing aspect of the medication is its persistence in the stomach as evidenced by gastroscopic examination. Patients find it unnecessary to take this medication every two hours or less, except at onset of therapy in some cases.

It was not necessary for the patients to take the test medication more frequently than every three or four hours. We also found it possible to maintain the patients on one tablet 4 times daily after initial intensive medication.

ILLUSTRATIVE CASE REPORTS

The following cases illustrate typical effects of the antacid-mucoid combination on the clinical manifestations and the gastric acid contents of treated patients.

Case 1:—S. T., female, age 41. Duodenal ulcer diagnosed clinically and by x-ray. There was a 10-year history of typically recurring symptoms due to duodenal ulcer. Treatment with 2 tablets every 2 hours was instituted, plus milk feedings and a bland diet. After 2 weeks, the tablets were taken every 4 hours

TABLE I
RESPONSE TO COMBINED ANTACID-GUAR CELLUPECTINOID (BALVIS) THERAPY

Diagnoses	Number of Cases	Responses		
		Excellent	Fair	Poor
Duodenal ulcer	66			
Gastric ulcer	5			
Hypertrophic	7			
Total	78	63 (81%)	8 (10%)	7 (9%)

for an additional 6 weeks. Complete relief of all symptoms was obtained and the patient has continued on a bland diet. Gastric analyses made with the Ewald Test Meal showed the results in Table II.

Case 2:—D. M., male, age 41. Duodenal ulcer of 7 years' duration, confirmed by x-ray. Pain is moderately severe. Administration of 2 tablets of the control preparation (antacids alone) every 2 hours, together with frequent milk feedings and a bland diet, produced only mild relief of pain. Before the 2-hour interval was up, the patient began to experience recurrence of pain. The patient was then given the combined medication (Balvis) every 2 hours and no recurrence of pain was noted. After 2 weeks the patient was placed on a 4-hourly dosage schedule of 2 tablets per dose for 2 additional weeks, then 1 tablet every 4 hours. This was continued for 3 months, with no recurrence of pain, and with satisfactory weight gain. Gastric analyses with Ewald Test Meal showed the effects on gastric acidity indicated in Table III.

Side-effects:—On a dosage of 2 tablets every 2 hours, there occurred 2 cases of diarrhea, 6 of marked constipation, and 9 of moderate constipation. None of these occurred on a 4-hourly dosage schedule.

COMMENT

It is evident that incorporation of the mucin-like component, guar cellupectinoid, prolongs the action of antacid medication. This was shown by the greater duration of relief from pain, as compared to controls in which the only variable was the omission of the mucoid, and by objective, gastroscopic evidence of retention of the antacid-mucoid preparation.

During recent years, the importance of mucin as a factor in the body's defenses against ulceration has become increasingly apparent. It has been shown

TABLE II

	Before Treatment		After Treatment	
	Fasting	2 hours	Fasting	2 hours
Volume of acid (c.c.)	70	30	25	20
Free	22	40	12	20
Total	32	58	24	32

that certain uronic acid-rich polysaccharides may overcome deficiencies leading to breakdown in mucin formation, and that these complex substances inhibit the formation of ulcers⁸. Both human gastric mucin and guar cellupectinoid yield uronic acids—chiefly glucuronic and galacturonic acids upon hydrolysis; and both are equally capable of combining with and neutralizing toxins. Guar cellupectinoid has nearly twice the viscosity of animal mucin. This viscosity may, conceivably, account for its tenacity in adhering to the gastric mucosa.

TABLE III

	Before Treatment		After Treatment	
	Fasting	2 hours	Fasting	2 hours
Volume of acid (c.c.)	120	44	42	18
Free	60	44	28	18
Total	88	62	40	36

It is of interest that studies using the Shay rat technic demonstrated the ability of the antacid-mucoid combination (Balvis) to aid in preventing ulcer formation. Figures 1a and 1b, illustrate the resistance of the mucosa in a typical Shay rat study.

A word about side-effects appears to be in order. Instances of both diarrhea and of constipation occurred in patients while on intensive dosage schedules.

On the other hand, the absence of either diarrhea or constipation in patients on maintenance dosages suggests that the combination of antacids in Balvis is relatively free of these undesirable effects.

SUMMARY

Seventy-eight cases of duodenal ulcer, gastric ulcer, and hyperacidity associated with hypertrophic gastritis were treated with an antacid-guar cellupectinoid combination, together with a dietary regimen. In 36 cases an initial control study was performed in which the only omission was the guar cellupectinoid component.

The patients receiving the antacid-mucoid complex (Balvis) obtained significantly better and more prolonged relief than those on control therapy. Gastroscopic examination of 4 patients on both Balvis and control medication revealed that the mucoid adjunct resulted in markedly longer gastric retention of the medication. This furnished objective evidence of prolonged duration of effect.

On maintenance doses of 4 tablets daily, neither constipation nor diarrhea was observed in patients receiving the antacid-mucoid complex.

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COMMUNAL MEDICAL CARE; A STUDY OF ITS ORIGINS

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The data of interest pertaining to the subject under discussion and the sources of information are not equally rich. It seemed expedient to do the grouping of the material available in alphabetical order of the various civilizations concerned.

ANCIENT ASSYRIA AND BABYLONIA

Almost our entire knowledge about Assyrian medicine derives from cuneiform texts found in the form of clay-tablets in the library at Nineveh of King Assurbanipal who reigned 669-626 B.C.

While the more ancient Assyrian medicine was purely sacerdotal and ritualistic, the more recent texts at least betray some scientific tendencies. There is nowhere, however, in the enormous number of medical texts even as much as a hint of what would resemble organized medical care of the people.

One author (McKenzie, 1924) maintains that incubation, or temple sleep, was already practiced in the Assyrian temples. This is an important statement as incubation has to be considered as the earliest, though very primitive medical treatment of diseased persons within an institution. The institution was a temple dedicated to the respective deity of health; the healers were priests, more or less medically trained; the treatment consisted, at least in the early times, mainly in what today we would call psychotherapy. We know that it was also practiced in ancient Egypt and, later on, came into use in Greece where incubation became a common procedure in the temples dedicated to Asclepius, the healing god of the Greeks.

While Herodotus's statement ("History", I:197) that the early Babylonians had no physicians at all is now completely discarded (A. C. Thompson, 1923, 1924, 1926), we do not find anything resembling public medical care in the Code of Hammurabi (ca. 2200 B.C.). Medically it contains nothing other than laws concerning payments to physicians for various successful treatments, and punishments when the treatment was unsuccessful. We are, therefore, at a loss to understand the assertions which we encounter in the literature (e.g. Meyer-Steineg and Sudhoff 1950) that the priest-physician at Hammurabi's time was an official of, and drew a salary from the king for which he "probably" was obliged to render his services gratuitously to the people. Nothing of this kind is found in the original text of Hammurabi's Code (translation by W. Eilers, 1932). Neither do we see any justification for the laudatory statement (King, 1910) that "its provisions reflected the king's own enthusiasm in the cause of

the humbler and oppressed classes of his subjects". There is not a word, directly or indirectly indicating such an enthusiasm, in Hammurabi's Code.

Furthermore we are told that "a university, chiefly celebrated as a medical school, existed at Borsippa, near Babylon." (Sayce, 1885, 1900; Meyer-Steinig and Sudhoff, 1950). This statement is based probably on Strabo ("Geography" B.16, Ch.1), and definitely on the fragment of an old medical work, now in the British Museum. What Strabo actually said, was this: "There are various kinds of Chaldaean (that is, Babylonian) astronomers—among them those of Borsippa—who, divided, as it were, into schools, teach different doctrines about the same subjects". And the old medical work just mentioned says only this: "... recovery thro' the master of the thumb (or lancet?), the road to Borsippa, a complete strengthening, the potent medicines of Adar and Gula as many as exist on tablets, I wrote, I engraved, I made clear, and for the inspection of my readers within the palace I placed". (Quoted by Sayce, 1885, in translation from the original.)

The conclusions drawn from these two passages (by the authors mentioned above) do not seem to be justified; nor does the additional hypothesis of Sayce (1885) that "the temple of Nebo at Borsippa perhaps was a Babylonian temple of Aesculapius to which sick persons were carried. . ."

The clay-tablets found in Nineveh represent for the most part copies made from older Babylonian originals (Jastrow, 1913-14) while the medical section is entirely of Babylonian origin. The contents mainly refer to incantations and divination-practices; actual medical treatment plays a minor role, at least in the early Babylonian texts. Nowhere in them is any indication found that the ancient Babylonians had even a rudimentary form of public medical service. In general, it may be said that the medical service to the King was as good as it was poor to the common people (Meissner, 1925).

Certain monasteries at Hammurabi's time seem to have issued provisions ordering their inmates to care for, and maintain sick women, particularly priestesses. They may even have had departments for the care of patients (Meissner, 1925). Provided that this was really so, these Babylonian cloisters would represent the earliest predecessors of the convent-hospitals that began to flourish in the early Christian centuries.

ANCIENT CEYLON

The medical history of Ceylon is deposited in the chronicle "Mahavamsa" which contains the more recent "Culavamsa" (both translated by Geiger, 1929 and 1950, respectively). These scriptures deserve our particular attention within the frame of our subject.

The Mahavamsa tells us that King Pandukabhaya as early as the 4th century B.C. built a hospital in his capital Anuradhapura, lying-in shelters in several

places, and also a convalescent home. We find in the Mahavamsa also the record of King Duttha gamini (101-77 B.C.) who bestowed food and remedies upon the sick, following the example of a preceding king (247 B.C.) who had set up "tanks with remedies for the sick at the city gates." King Duttha gamini is also said "to have erected in 18 places infirmaries provided with sufficient means, medicines and professional care for the treatment of sufferers." (Puschmann 1891, Withington 1894). We read further in the Mahavamsa that the Singhalese King Budhadasa in the 4th century B.C. instituted a Public Health Organization in his country. He provided hospitals and appointed medical practitioners for all villages in the land, one physician for every 10 villages. He even conferred the income of 20 royal villages on these physicians as means of their maintenance.

In the Culavamsa there is a long list of Singhalese kings who in the first millenium of our era erected "nursing shelters" (Upatissa II, 375 A.D.), "large halls for the sick, the cripples and the blind" (Udaya I, 901 A.D.), hospitals (Kassapa IV, 912 A.D. and Kassapa V, 929 A.D.). Mahinda IV (975 A.D.) distributed medicine and beds in all the hospitals. His son built a hospital for the laity in town. Most outstanding, however, was the King Jarakramabahu I (1153-86), "He made provision for the maintenance of wise and learned physicians. He had a great hall built for many hundreds of sick people and had placed in it a complete collection of useful articles. He also gave to each sick person a special slave and, in addition, a female slave to prepare—medicine and food—".

These early humanitarian activities are not surprising when we remember that kings of Ceylon and its whole population embraced Buddhism in the middle of the 3rd century B.C. The practical outcome of Buddha's teachings was the early setting up of institutions which were destined to relieve, or at least alleviate, the misery of the people by giving easy and free access to ambulatory and hospital treatment to as many as possible.

ANCIENT AND MIDDLE AGE CHINA

A short note in No. 122 of the Technical Reports of the World Health Organization (1957) states that free clinics for the sick were established early in ancient China. According to Wong and Lien Teh (1936) the "Chou Ritual", a chronicle referring to the time of the Chou Dynasty (1182-255 B.C.), and written at an uncertain later time (I. Veith 1943) reports that, as early as the 10th century B.C. the four groups of medical men employed in the health service (physicians, surgeons, dietitians and veterinary surgeons) were paid out of public funds and received their salaries at the end of the year, "each physician getting as much as the result of his work justified". In a separate earlier paper, Wong 1923 quotes from the "Chou Ritual" as follows: "... the patients are sent to the different departments to be treated," and he infers from this passage that

governmental free clinics were already in existence at the early time to which the "Chou Rituals" refer.

It is of interest that these early medical performances were used by Wang Au-Shih, a social reformer of the 11th century A.D., as a support for his own reformatory ideas. "He wanted to make sure that everyone, regardless of social standing, would receive medical attention". (Ilza Veith 1943). Hospitals as already in existence in the Chou period were mentioned by the Taoist philosopher Kwan Tzu who, probably about 300 B.C. (Hübotter, 1929) wrote: "In the capital there are institutions where the deaf, the blind, the dumb, the lame, the paralytic, the deformed and the insane are received. When ill they are cared for until they have recovered."

While many such references are said to be found in the records of later dynasties, we do not know how these places were equipped and managed. It is believed that their standard was very low. Examples of several such hospitals are given by Wong and Lien Teh. Only one, referred to in a royal proclamation of the Wei Annals (60 A.D.) may be quoted here, "Be it ordered that the Master of the Great Banner shall establish a hospital in some suitable place and send all the suffering people there. Be it further ordered that the Medical Bureau shall assign doctors to treat them. . ." (Wong, 1923).

In the 6th century A.D. Buddhism was firmly established in China and hospitals in connection with Buddhist monasteries were common. Each province had at least one such hospital (W.H.O., 1957)*. A record of the "Tung History", dated 1102 A.D., says that the prefect of Changhow founded the "Benevolent Institute for Sick People" where patients were treated free of charge.

In 1299, by order of the Emperor Ta Teh, "2 doctors were appointed to each of the larger hospitals and 1 to every small hospital. The amount of revenue appropriated was based on the population of the district". (Wong and Lien Teh, l.c.). A later edict issued during the Yuan Dynasty (14th century A.D.) refers to the foundation of "a dispensary which was entirely maintained by governmental funds out of which skillful physicians were salaried and the necessary remedies provided." (Wong and Lien Teh, l.c.).

Thus it cannot be denied that in China from early times on there was already an understanding for the needs of the sick and the germ of the hospital idea was already budding.

ANCIENT EGYPT

Our chief sources of knowledge regarding medicine of the ancient Egyptians are the Pharaonic medical papyri and the books of ancient writers, particularly Herodotus and Diodorus Siculus. The medical papyri (most important

*See also: P. Huard et Wong, "Le Bouddhisme et la Médecine Chinoise", Histoire de la Méd., Paris, 1958.

the surgical papyrus Edwin Smith, the papyrus Ebers, the Berlin medical papyrus and the London papyrus) are invaluable storehouses of ancient Egyptian medical science. Though closely interwoven with magic (Hurry, 1928), they give clear insight into the rather advanced and often surprisingly good medical knowledge at a period as early as about 1500 B.C. They are not, however, contributory to our subject. Neither is Herodotus in the passages which deal with Egyptian medicine (History, Book II, ch. 77; ch. 84; Book III, ch. 1; ch. 129); only his statement (Bk. II, ch. 84) that the Egyptian physicians were all specialists may be mentioned here. Diodorus, on the other hand, tells us (Historical Libr. Bk. I, ch. 82) of free medical treatment in ancient Egypt by physicians who were paid for their services by the State. The singularity of this statement, no matter how precise, is not very conducive to its credibility.

In the most ancient times the temples of the God Toth in Heliopolis, Memphis, Thebes and Sais were dedicated to the study of, and the care for, the sick by the priests who alone had medical knowledge. Later on, incubation for healing purposes was practiced in the Temple of Imhotep at Memphis (Hurry, 1928), long before this was done in the Aesculapia in Greece (Gask, 1939). The court physicians of the Pharaohs were at the same time the heads of staff of the physicians working in these temple-hospitals. Their names and titles are found inscribed on many stele still extant (McKenzie, 1924).

The Pharaonic Empire came to its definite end in 332 B.C. through the victory of Alexander the Great and became a kingdom in 305 B.C. under one of Alexander's generals, Ptolemaeus Lagi. Ptolemaic Egypt (305-31 B.C.) remained essentially Egyptian in spite of its hellenistic government, army and administration. The papyri of that epoch were written in Greek and form, together with those of the subsequent Roman period, which were also written in the Greek language, the most important sources of present-day information.

According to Rostovtzeff (1941), "physicians played an important role in the life of the eastern monarchies. The Ptolemies appear to have created what was the first State Sanitary Service and Socialized System of Medical Assistance of which we have evidence in the history of civilized mankind." Among the evidence for such a weighty statement there is a Delian inscription of the 2nd century B.C. in which we read that a certain Chrysermus was the chief of the doctors practicing in Alexandria. From Greek papyri we know that the Ptolemaic public physician was carefully supervised and that a special tax (*Iatrikon*), as in the Greek city-states, was levied from all the inhabitants of the country to pay for the general medical assistance. Numerous tax records referring to the payment of this tax in Ptolemaic Egypt are preserved (Woodhead, 1952). Strangers and visitors enjoyed, as in Greece, the privilege of being treated without cost by the public physicians (Diodorus Siculus I, 82). It is highly probable that Alexandria, the Ptolemaic capital, and the rest of the country had separate health services under separate administrations. The doctors in the service outside of Alexandria

were called "Royal doctors" and their chief function probably was to attend to the health of the Egyptian population. The doctors, like many other officials in the service of the government, were considered as "specialists" (*technitai*); they lived on modest salaries.

Conditions did not change much after Egypt had become a Roman province. Public physicians are still mentioned in papyri of the 2nd and 3rd century A.D. (*Oxyrhynchi Papyri*, Greenfell and Hunt, vol.I:40 and 51; vol.III:475). The designation of public physician ("Royal physician" in Ptolemaic Egypt) as "*archiateros*", a title originally given to the court physicians of the Seleucid Kings in Syria (2nd century B.C.), came in use much later for the public physicians in the Roman Empire (Gummerus, 1932). Oehler (1909) maintains that the term "*archiateros*" appears quite late in Roman Egypt. Rostovtzeff (1941), however, tells us that this title was already used, occasionally, in Ptolemaic Egypt, in the 1st century B.C., but seems to have been abolished in Roman Egypt.

The institution of public physicians in Egypt had to be referred to in this section because it was an integral part of the sanitary system of Ptolemaic and Roman Egypt. It is, in fact, a Greek conception and more has to be said about it in the next section, dealing with Greek Medicine.

ANCIENT GREECE

The so-called *Asclepieia* were originally temples of Asclepios, the Greek god of the healing art, and gradually became places to which ill people flocked, expecting a cure from the means of treatment available there: prayer and incubation (Hamilton, 1906), later also medical treatment and surgery. The rational part of the cures in the *Asclepieia* goes back to Alcmaeon of Croton (ca 500 B.C.) who was a pupil of Pythagoras. Subsequent to the migration of the Jonian philosophers from Asia Minor to Greece, Italy and Sicily, medical institutions attached to the temples of Asclepios grew up there in many places in the course of the 5th century B.C. Among them was the famous *Asclepieion* on the island of Cos where Hippocrates is said to have studied and worked at the end of the 5th century B.C.

In the course of time the exclusive connection of physicians with the *asclepieia* loosened or even ceased, and the Greek physicians worked in places of their own, the so-called *iatreia*. These institutions came into being in the 4th century B.C.; though privately owned by the physicians they were subsidized by the communities. They were usually attached to the doctor's residence and had facilities permitting routine medical, even surgical, treatment. The patients sometimes stayed in these places for a considerable period of time. Hippocrates gave exact prescriptions concerning situation, equipment, etc., of these *iatreia*.

The opinion that Hippocrates drew his wisdom from the work in the *Aesculapium* at Cos is nowadays energetically opposed (Gask, 1939). Be this

as it may, the one fact has been firmly established, by excavations principally at Cos, Epidaurus and Athens, that those Asclepieia were something like fore-runners of our hospitals and, if nothing more, at least comparable to our spas. Buck (1917) calls them "the prototypes of our hospitals" while Gask and Todd (1953) deny any such resemblance. Perhaps they were the first form of the Christian hospitals when in early Christian times they were taken over by the Church along with the pagan temples (Edelstein, 1945, vol.II:176). For literature relevant to their topographical layout and purposeful arrangement see Ciba Ztschr. No.85,Bd.8 1957.

The numerous inscriptions on slabs of stone found in the ruins of many asclepieia form the epigraphic evidence for the assumption that the institution of "public physicians" was common in Greece at the end of the 5th century B.C. and that these public physicians were paid for their services by the communities which levied a special tax, the "iatrikon" on their citizens for this special purpose (cf. Pohl, 1905; Rostovtzeff, 1941; Meyer-Steineg and Sudhoff, 1950; Woodhead, 1952). We have already encountered this tax in the discussion of public medicine in Ptolemaic Egypt where it was introduced from Greece.

The inscription No. 437 in the *Sylloge Inscriptionum Graecorum* ca 263 B.C. (Dittenberger, vol.I) says that "the Delphic assembly granted to a certain Philistion and his descendants exemption from certain duties and taxes, including the iatrikon" (cf. also Woodhead, 1952). Dittenberger annotates another inscription (i.e., No. 335) which refers to the praise by the Athenians of a public physician after many years of service, as follows: "The public physicians were elected by the Greeks either by lot or handsign. These doctors treated the patients free of charge and did not accept any money from them. For that particular reason it was customary to grant them the living expenses out of public funds" (translation from Dittenberger's Latin Text).

R. Herzog (1899) tells us of an inscription which was found in Cos and confirms the existence of the iatrikon. He furthermore quotes the fragment of an inscription which stipulated that the community of Teios exempted new citizens from paying certain taxes, the iatrikon excepted. He also refers to an inscription (Dittenberger, l.c., No. 313) which would indicate that the community of Delphi equally paid their physicians out of a communal tax. I was unable to find this inscription in Dittenberger's work and have to be satisfied with Herzog's authority. The existence of such a communal tax has been known to historians for almost 100 years. We find the following passage in a review of an archeological report of G. Perrot, Paris 1862: "Among the interesting details which lately have become known in relation to the medical service of the Greeks . . . the exemption from the public health contribution is mentioned. This permits the conclusion that the Greek communities contributed regularly to the pay of doctors and the maintenance of medical institutions." (Curtius, 1865).

Paton and Hicks (1891) mention an inscription (No. 5) discovered at Cos following which a golden crown was conferred on a public physician as reward for his services during an epidemic. Inscription 344 of the same authors renders a similar decree in honor of another deserving public physician. And finally, an inscription of the 3rd century B.C. was found on the island of Carpathos that runs as follows: "considering that Menocritos—during his activities as a public physician over more than 20 years never stopped treating everyone with zeal and devotion. . . ., considering that he preferred a life of poverty to the acceptance of a salary, and considering that he never hesitated to visit even those patients who lived far out in the outskirts of the town, the citizens of Bryconthe have decided to bestow upon Menocritos their praise and a crown of gold, and to erect—a stele of marble with the inscription of this decree in honor of his knowledge and his virtue—" (translated from Wescher, 1863).

In the classical literature, Aristophanes in his comedy "Ploutos" speaks of the public physician in Athens in a derogatory way, claiming that his art degenerated in the same degree as his salary was reduced. (Translated by Quinn, 1896;14). In another play, the "Acharnians", Aristophanes speaks of the "parish doctor" or district medical officer, and Starkie (1909) in his translation of the play annotates this famous passage by saying that "a certain number of doctors were elected every year who received a salary from the State and attended the poor without fee."

Herodotus ("History", Bk.III,Ch.129) narrates the biography of the physician Democedes who lived in the 6th century B.C. and became medical officer with a successively increasing salary in Aegina, Athens and Samos: "—The State of Aegina hired his services at the price of a talent annually (ca \$680.); then the Athenians engaged him at 100 minae (ca \$1130.); later Polycrates of Samos paid him 2 talents (ca \$1370.)." Democedes was most effective as a surgeon and probably represents the earliest historical Greek practitioner known. Skemp (1952) calls Democedes an exceptional character and remarks that "the usual practice—appears to have been election by the respective State of one or more of these public physicians. The State paid the salary and their duties seem to have included treatment of the war-wounded and dealing with epidemics."

Diodorus Siculus, a Greek historian in the time of Caesar and Augustus, asserts (Hist. Libr., Bk.XII,ch.13) that in Greece in the 7th century B.C. laws already existed that ordered treatment of ill persons by physicians at public expense: ". . . Charondas (an old law-giver of the late 7th and early 6th century B.C.), believing as he did that the illiterate were being deprived of certain great advantages, by his legislation corrected this wrong and judged them to be deserving of concern and expense on the part of the State; and he so far excelled former law-givers who had required that private citizens when ill should enjoy the service of physicians at State expense that whereas those legis-

lators judged men's bodies to be worthy of healing, he gave healing, to the souls which were in distress through want of education."

As high an authority as Plato can finally be produced as a witness. There is a passage in *Gorgias* (X, translation of Plaistowe, p. 16) that refers to the election of public physicians: "Whenever the City holds an assembly for the election of physicians—, will not the rhetorician refrain from giving his advice at such a time? Surely, he will; for evidently at each election we ought to choose the most skilfull man in his craft—". There is another relevant passage in the *"Statesman"* (Translation by Skemp, 1952, p.124): "Suppose we find a medical man who is not himself practising as a public medical officer but who nevertheless is competent to advise a doctor actually serving in that capacity?"

Plato's dicta ensure that the office of "Public Doctors" still existed in the 4th century B.C. We believe its continuance to be proven by the inscriptions and authors referred to above. We already encountered its transplantation into Ptolemaic Egypt. We shall hear more of it in the discussion dealing with medicine in the Roman Empire. These public physicians treated the people but were by law not allowed to take money from them. They received instead a salary that was modest as a rule (Tarn and Griffith, 1952).

Reference should be made here to a highly critical study of recent date (Cohn-Haft, 1956) that undertakes to shatter all the opinions and teachings on the institution of public physicians in ancient Greece. In spite of the thoroughness and cleverness with which the complicated material is presented, it seems to be very doubtful whether the author just mentioned will succeed in converting the general conviction to his own. The evidence being available and appealing to common sense is too strong in favor of the statement that "the system of a government-sponsored Health Service was common to all Greek States from the earliest to the latest periods of their history" (Woodhead, 1952).

INDIA

Care and treatment of the sick is said to have been one of the duties of the government in the reign of the Indian Emperor Chandragupta Maurya, 322-298 B.C. (cf. Muthu, 1930). Even medical plants and herbs were cultivated by the State to the benefit of the people. Kautilya, the Prime Minister of Chandragupta, in his law book *Arthasastra* regulated in minute detail all matters of worldly life, including medicine (Muthu, 1930). We are even told that the erection of medically staffed hospitals at the chief centers of the country was due to his initiative (Nehru, 1947; Majumdar 1952). Nothing, however, regarding the erection of hospitals can be found on perusal of the *Arthasastra* (translation by T. T. Meyer, 1925). Registration of births and deaths, obligatory report of dangerous diseases, extermination of pests, supervision of prostitutes, even medicolegal autopsies were strictly ordered by medical boards and enforced by executive

organs (Castiglioni, 1947; Rawlinson, 1952). Good nursing was insisted upon and considered "the fourth leg of the art of healing" (Zimmer, 1948).

Emperor Asoka (247-236 B.C.), the grandson of Chandragupta Maurya and fervent adherent of Buddhism, already recognized that "one of the chief evils of poverty is that the poor man cannot get a physician or the medicine he needs" (Withington, 1894). Free treatment for all living beings, human and animals alike, was therefore instituted by him throughout his Empire (Hemmeter, 1936; Reddy, 1941; Zimmer, 1948 and many others). We know in full the organization of social medicine under Asoka through his custom of rendering account of his ordinances and achievements by inscribing them on rocks. Thirty-four of these rock-edicts are preserved. Most interesting to us is the second which runs as follows: "Everywhere in the Empire . . . the King erected two kinds of hospitals; hospitals for human beings and hospitals for animals. . . ." (Bühler, 1883).

Nearly 600 years after Asoka, the era of the imperial Guptas started with Chandragupta I who ascended the throne 320 A.D. and rallied the Indian Empire to new heights. We know from the reports of the Chinese pilgrim Fa-Hsien who toured the Gupta Empire between 405 and 411 that India at that time enjoyed generous endowments of social service (Mookerji, 1947). The imperial Guptas took care that all villages were provided with physicians. Hospitals were set up according to Fa-Hsien's testimony (transl. by Legge, 1886): "The heads of the Vaisya families establish houses for dispensing charities and medicines. All the poor and destitute in the country, orphans, widows and childless men, maimed people and cripples, and all who are diseased go to those houses and are provided with every kind of help, and doctors examine their diseases. They get the food and medicines which their cases require and are made to feel at ease." This hospital which Fa-Hsien found at Pataliputra may have been "the earliest public hospital in the world that was maintained by the State and public subscriptions" (Chakravarti, 1952; Gokhale, 1952).

Some information pertaining to our subject is gained by study of Kalhana's *Chronicle of the Kings of Kashmir* (transl. by Stein, 1900; see also Heusinger, 1847) which was written in the 12th century A.D. It is supposed to be a reliable historical work (Majumdar, 1952) and it informs us about the foundation of several hospitals in Kashmir: King Ranaditya erected a "faultless" hospital in the 3rd century A.D. (l.c. vol.I, Bk.2, v.58), the King Baladitya also founded a hospice for the accommodation of his subjects in case of disease.

Only short reference can be made here to the epigraphical and literary evidence proving the existence of dispensaries and hospitals in South India before and after 1000 A.D. Although not much evidence is left for the period before 1000 A.D., little doubt is permitted as to the provision of at least some sort of medical relief. The epigraphical evidence, however, becomes conclusive with the early 11th century A.D. and confirms the existence of dispensaries

and hospitals in South India even before its contact with Islam and the European Renaissance. Extensive details referring to this subject can be found in the important paper of Reddy (1941). The Tirmukkudal-inscription, the most important medical inscription of South India, is given here as an example out of the wealth of information contained in Reddy's paper. This inscription dates from the 11th century A.D. and contains the grant given to the hospital and the details of its equipment. Another example is the inscription which was found in the Vishnu temple of Venkateswara Pertumal and refers to the hospital attached to it. This hospital "was provided with 15 beds for in-patients. Only the seriously ill were accommodated in the hospital." No information is given regarding the number of out-patients and the names, frequency or incidence of diseases treated. The staff was adequate and consisted of the chief physician whose name is given, one surgeon, two pharmacists, two nurses, and the menial staff including watermen, barber, cook and porter (Reddy, l.c.).

In the centuries of Islamic rule over India we hear little of medical care for the people. Generally, the medical care for the subjects of the Mogul tyrants was highly inadequate.

ISLAM

The first hospital in Islam was that erected 707 A.D. by the Caliph el Walid ben Abd el Malik (705-715). Other Umajjads built smaller hospitals for lepers and blind people.

Medicine developed tremendously when the Abbasid Caliphs, beginning with Harun al-Rashid (766-809), ordered and sponsored the translation of Greek besides Indian medical writers. Quite a few of those Caliphs were, in addition, great hospital builders and philanthropists. They founded many hospitals in Baghdad and the provinces, all well organized and provided for with medical and nursing staff (Castiglioni, 1947). As early as the days of the Caliph al Mamun (813-834), there was regular inspection of the pharmacies in Baghdad and the whole empire (Khairallah, 1946). Cordoba, in the western Caliphate, had from the 8th century onward a university which in the 10th century was closely associated with 50 hospitals (W.H.O., 1957). The Jewish physician and traveller Benjamin of Tudela reported in 1160 that gratuitous treatment in the Islamic hospitals at Baghdad and in the provinces was provided for (Elgood, 1951). Under the Caliph Muhammad al Qahir (early 10th century) the outstanding physician Sinan I of the Qurra family is said to have raised the Public Health Service and the Hospital Administration in Baghdad to perfection (Elgood, l.c.). The insane in those times were considered as dependent on public charity (Khairallah, 1946).

Feudal as society in Islamic countries then was, with relatively few in power and the vast majority of the people underprivileged and poor, these many

hospitals must have been built in the first line for those who could not afford medical treatment if they had to pay for it themselves.

There are, in spite of an extensive literature, both ancient and modern, no means for us to know what the impact of the Islamic achievements in medicine upon the health conditions of the broad masses actually was. They seem to be most important inasmuch as modern medicine, and social medicine as its most recent branch, undoubtedly would have been forced to start completely anew, if the translators at the Islamic court, who were outstanding clinicians at the same time, had not kept alive the medical knowledge of the Greeks, and if the medical schools which formed in various European countries under Islamic rule and influence (Salerno, Toledo, Palermo, Montpellier, Bologna, a.o.) had not taught medicine as they had learnt it, through Rhazes and Avicenna, from Hippocrates and Galen.

JAPAN

The little that we know about the earliest history of medicine in Japan derives from three chronicle books (*Kojiki*, *Nihongi*, *Fudoki*) which were written as late as the 8th century A.D. and are not too reliable for that reason alone.

Medicine of some value was imported into Japan first from Korea and China, together with the Mahayana Buddhism, in the 6th century A.D. The Buddhist monks, in the wake of their missionary activities, founded hospitals with attached out-patient departments the earliest of which is said to have been established in Osaka in 593 A.D. During the so-called Nara-Period (710-784) there existed in every province a hospital and a dispensary, both connected with a buddhist monastery (W.H.O. Report, 1957). A charity hospital was founded in 758 A.D. at the order of the Empress Komyo, who is said to have treated the leprous herself in a medicinal bath. From Fujikawa (1924, 1937), we learn that *Ishinho*, the oldest existing medical book of Japan (982 A.D.) already described hospitals for the exclusive care and treatment of patients suffering from the dreaded *Variola*. *Ninsho* (Kamakura period 1187-1333) founded a leper home in Nara at the end of the 13th century and, somewhat later, a large hospital for the poor.

Medical care for the masses in ancient Japan seems to have been sporadic, to put it benevolently. The ruling classes permitted, if they did not directly oppose, the religious and later the commercial functionaries from abroad to do for the health of the people what they could, which was a necessity on a limited scale. This has fundamentally changed in our times.

MEDICINE OF THE JEWS

Under Medicine of the Jews, we have to understand first the medical laws of the Old Testament which were part of the theurgic law-book of the ancient

Jewish State and, second, those of the Talmud which originated in the 1st century A.D. and found its final revision in the Talmud of Babylon in the 6th century A.D. The Talmud with its commentaries has been forming the religious law-book of orthodox Jewry ever since.

Though much could be said about the laws of Public Hygiene contained in the Old Testament, little is found there that would resemble our modern conception of medical help to the diseased individual by public or semi-public agencies. There are but a few passages in the Bible where physicians are mentioned at all (II Chron., ch.16,v.12; Jerem., ch.8,v.22; Jesus Sirach, ch.10,v.11; ch.38,v.1-15). The Old Testament refers much more frequently to a kind of priest-physicians (Levites) who were, by religious law, the officials of Public Hygiene and, as such, charged with observation and isolation of diseased persons, and those suspect of disease (Levit., ch.14).

The Public Health Laws are numerous and variegated; many of them can be traced back through Egyptian papyri, to Pharaonic times (Osler, 1922; Barach, 1928). There are among others dietary laws (Levit., ch. 3 and ff.), funeral laws (Gen., ch.25,v.9; Judges, ch.16,v.31; Jos., ch.24,v.32), laws against prostitution and perversion (Gen., ch.38,v.24; Exod. ch.22,v.18; Levit., ch.20, v.13 & 15; ch.18,v.6-18), laws regulating clothing and body hygiene (Eccl., ch.9, v.8; Levit., ch.15,v.5 ff.; II Kings, ch.5,v.10,12), laws for prevention of infectious diseases, particularly lepra (Levit., ch.13,v.2, ff. and v.45; ch.14,v.32 ff.; II Kings, ch.7,v.3; II Chron., ch. 26,v.21; II Kings, ch.15,v.5), regulations for prevention of childbed-fever (Levit., ch.12) etc. There was even a law for the laying out of latrines (Deut., ch.23,v.13 ff.).

The medicine of the Talmud is not fundamentally different from that of the Old Testament. The general rules in dietetics and general hygiene were commented upon and stressed; diseases were no longer considered necessarily and exclusively the outcome of sin (Loewe, 1911). The natural and medical sciences assimilated valuable information from Greek and other sources.

The Jews, beginning with Moses, may be, therefore, considered as the creators of the science of Public Hygiene (Baas, 1889). It is the more surprising that, in the course of their history, we do not hear much of anything near socialized medicine. Neither did they build hospitals on any appreciative scale. There was, in biblical times, "a house set apart" for the leprous King Uzziah (II Chron., ch.26,v.21). Jewish homes for sick travellers are often mentioned in the Talmud. They were particularly frequent in Jewish communities after the Crusades and first designated as "hospitale judaeorum" ("Hekdesh") in Cologne, in the 11th century A.D. (Jew. Encycl., 1925). In favor of the opinion that the Jewish hospice of this type was as old as, or even older, than the equivalent Christian institutions, a letter of St. Jerome to the Roman lady Fabiola (Epist., 66) is quoted in the rabbinical literature. In this letter St. Jerome referred to Abraham who according to rabbinical tradition built under the oak at Hebron

and the Terebrinth of Beersheba an inn for strangers: "I am happy to see a branch of Abraham's Terebrinth transplanted to the East", (Univ. Jew. Encycl., 1948).

PERSIAN MEDICINE

Early Persian medicine is Zoroastrian in origin. Certain parts of the Avesta, the Zoroastrian Bible, which originated about 600 B.C., contain details about medicine and physicians. Of these the Vendidad and the Hushpam Nask are preserved in the much later Zend language; the original version of the Avesta was destroyed by Alexander the Great when he burned Persepolis in 330 B.C.

Like Assyrian medicine, early Persian medicine was based upon the belief in demoniacal possession as the cause of disease. The healing art was practiced by priests and magi. Airyaman, the Zoroastrian "Genius of Health" cured with holy formulas (Dhalla, 1938). The sanitary laws of the Vendidad aimed at prevention of contagious and infectious diseases (Kanga, 1906). They tried to achieve this by strictest isolation of everybody and everything unclean, and by rigid purifying methods. There were three kinds of healers, the most valuable of whom was believed the one who healed by the aid of spells (Benveniste, 1945). The others were those who healed with the knife and with drugs, respectively.

In early Persia it was the duty of the rulers to found hospitals and to provide them with drugs and physicians (Elgood, 1951). It is, therefore, not surprising to read in the Dincard, a later (9th century A.D.) Pahlavi-version of the Avesta, that "a good physician should be provided with an income that would enable him to live in a house in a prominent locality and furnished with the necessary furniture" (Quoted by Elgood l.c., p.177).

The greatest event in Persian medical history probably was the foundation of the Medical School of Jundi Shapur by the early Sassanide Shapur I in 260 A.D., and its subsequent development to real glory when the Nestorians, exiled as heretics from Byzanz and persecuted by the Church and the Emperors of East Rome, fled to Persia in the 5th century A.D. and obtained asylum there. They transformed the already existing school at Jundi Shapur into an outstanding centre of theoretical and practical medicine. The school attained its greatest height under Chosroes I (531-579), the most brilliant of the Sassanides.

We owe an excellent monograph of rather recent date, dealing with this ancient university, to Brody (1955) and we learn from it, as from other sources, that medical science and hospital facilities at that institution were so far advanced that the Abasside Caliphs after their conquest of Persia in 636 A.D. not only modelled their hospitals in Baghdad on it but also called upon its physicians and professors to staff these hospitals and to serve at the same time as their court physicians.

While Greek medicine became stale and scholastic in Baghdad and elsewhere, the germs of progress cultivated at Jundi Shapur were revived in the 16th century and then formed the fundament of what we call today modern rational medicine. It is out of this type of medicine that modern medicine grew, and in its wake any modern medical system that attempts to provide help for the many.

ROMAN MEDICINE

Roman medicine from its beginnings until the division of the empire (395 A.D.):—The ancient Romans did not care much about professional treatment of their sick. The temples of Saturn, the Roman god of fertility and also of healing, are said to have been the earliest sites of medical instruction and practice in Rome. This is, however, purely legendary. Later, until about the time of M.P. Cato (234-149 B.C.), the *pater familias* acted as family doctor. "Cato himself had written a little book of prescriptions for curing those who were sick in his family. . . ." (Plutarch, Cato Major, vol.I). Often specially trained slaves were employed as physicians. The first real physician who ever practiced scientific medicine in ancient Rome was Archagathos, born and educated in Greece. He came to Rome in 219 B.C. and was provided with a "taberna" or "medicina" that was modelled after the Greek "iatreion"; he was paid for out of public funds (Pliny, Nat. Hist., Bk.29,ch.6). There is a passage in the comedy "Menaechmi" of the Roman playwright Plautus (254-184 B.C.) that at least proves the existence of such tabernae in Rome at his time. Plautus makes the physician, who is called to treat a man apparently suffering from an acute psychotic condition, say this: ". . . do you know what's the best for you to do? Have him taken to my house . . . there at my own discretion I shall be able to treat the man. . . . I will make him drink hellebore some twenty days . . . go fetch some man to take him off to my house. . . . I shall go home that the things may be got ready which are necessary to be prepared. Bid your servants carry him to my house. . . ." (Act V, transl. by Riley, London 1900).

Some authors deny, in spite of this passage, that the Roman iatreia had beds attached or provisions for nursing the sick (Gask and Todd, 1953).

Greek medicine became more and more leading in Rome, and in 154 B.C. the *Collegium Aesculapii et Hygieia*, consisting almost exclusively of Greeks and hellenized orientals, was erected. Certain schools formed on the basis of Greek science and medicine: the Methodists founded by Asclepiades (1st century B.C.) then the Eclectic Pneumatists and the related Encyclopedists with Galen (131-204 A.D.) as their most important representative. Even he was a Greek from Asia Minor (Pergamos) who settled in Rome but wrote in Greek. He reported that at his time many Roman towns, especially in the provinces, erected well-situated and lavishly equipped "tabernae" at their own cost and gave them to physicians for practicing their profession (Meyer-Steinig,

1912; for quotation from Galen see Puschmann, 1891). At about the same time the institution of public medical officers as it existed in Greece, was introduced into the Roman Empire. Their number depended upon the size of the town and they definitely existed already in Latium at the time of Trajan (98-117 A.D.). In late Imperial Rome one doctor was appointed for every district of the city. They had to attend the poor without being paid by them. They were consulted in epidemics and other increases of sickness and mortality (Cod. Theodos. XIII, iii,8, quoted by Woodhead, 1952).

In Roman Egypt the old Greek designations *demosios iatros* or *iatros demosieumon* were still used in the 2nd and 3rd centuries A.D. (Greenfell and Hunt, Oxyrhynch. Pap.I,40; I,51; III,475).

The title "Archiatros", originally used in Rome for the Imperial court physicians, came into use for the public physicians in the Roman Empire not before the 4th century A.D.

Short reference may be made here to founding asylums said to have been founded by the Emperor Nerva (96-98 A.D.), and to a hospital for parturient women erected at the site of a temple of Aesculapius at Epidaurus by the Emperor Antoninus Pius (138-161 A.D.). (Cf. Pausanias, *Descriptio Graecae*, II:27,1-7, quoted by Edelstein, 1945, vol. I, Testimonial 739).

The Roman talent of organization led to the erection of so-called "Valetudinaria" which were convalescent homes with sickrooms, built by the great landowners for treatment of their slaves mainly out of concern for their physical value (Columella, 1st century A.D., *De re Rustica* XI:1; XII:3; cf. also Seneca "Moral Essays", Loeb Class. Lib., vol.I,p.147). The Roman medical author Cornelius Celsus (1st century A.D.) wrote his book *De Medicina Libri Octo* as a manual for the managers of such institutions (Meyer-Steineg and Sudhoff, 1950). The management of these Valetudinaria was finally regulated by the Codex Theodosianus and promulgated 438 A.D. (Meyer-Steineg, 1912). Valetudinaria were also built for athletes and gladiators in imperial Rome (Castiglioni, 1947). Magnificent baths came into being and their maintenance was paid for by the State or the municipalities. When, from the time of Augustus (63 B.C.-14 A.D.), the Roman armies started to consist mainly of mercenaries, permanent army-physicians took care of them when they became ill or wounded. A few Roman military hospitals at the sites of army camps were re-discovered in our times (Carnutum nr. Vienna; Novaesium nr. the Rhine; both of the 1st century A.D.). The unearthed remnants prove their excellent and expedient arrangement (Meyer-Steineg, 1912).

Beginning with Constantine the Greek (324-337) Christianity had become strong enough to overcome the innate indifference of the Roman mentality toward the diseased individual. Christianized emperors, bishops and pious citi-

zens began to build hospital-like institutions, first mainly in the eastern provinces. With the beginning of the 4th century, after Constantine had closed the pagan asclepieia in 335 A.D., they extended this meritorious activity also to the western part of the empire. Many such "xenodochia", as they were called, are referred to in the literature* (cf. Baas, 1889; Sudhoff, 1913; Mercher, 1915; Hobson, 1926; Gask and Todd, 1953; Meyer-Steineg and Sudhoff, 1950; Ackerknecht, 1955, a.m.o.). We may assume that these institutions, or at least part of them, were already staffed with skilled medical assistants.

Most famous of all was the hospital at Caesarea, founded by Basileios the Great in 373 A.D. It was already a real, well organized general hospital (cf. Mercher, 1915; Meyer-Steineg and Sudhoff, 1950).

The welfare activities of the early church continued to grow in spite of the attempt made by the emperor Julian Apostata (361-363) to revive paganism and to suppress the new faith. He knew of no better device for attaining this goal than by establishing hospitals in every city of the empire "where the poor should be received without any invidious distinction of country or religion" (Gibbon, vol.II:375). Julian's letters are preserved and one of them runs as follows: "Why do we not observe that it is their (Scil. the Christians) benevolence to strangers . . . that has done most to increase atheism (ie. Christianity)? I believe that we ought really and truly to practice every one of these virtues. . . . In every city you must establish frequent hostels in order that strangers may profit by our benevolence: I do not mean for our own people only, but for others also who are in need of money. . . . It is disgraceful that, when no Jew ever has to beg, and the impious Galileans support not only their own poor but ours as well, all men see that our people lack aid from us. . . . Let us not, by allowing others to outdo us in good works, disgrace by such remissness, or rather utterly abandon the reverence due to the gods. . . ." (Letter to Arsacius, High Priest of Galatia, cf. Loeb's Cl. Lib. vol.III:69; also vol.II:337).

West Roman medicine from the division of the empire (395 A.D.) until the fall of West Rome (476 A.D.):—The Roman Empire was divided into East and West Rome by the Emperor Theodosius the Great in 395 A.D. At that time, the West Roman government and society had already become too weak and dis-solute to achieve anything of value in the pursuits of war and peace. The recurring invasions by barbaric armies, which even sacked Rome in 450 A.D., were, in addition, anything but favorable to the cultivation of the medical art. Initiative, power and wealth shifted to Byzanz which was still flourishing when West Rome had already perished for a long time. The only reference to major medical activities in the West Roman Empire between 395 and 476 is that to the

*Constantine the Greek: Great leper hospital in Constantinople; Zoticus: Xenodochium in Constantinople, 330 A.D.; Bishop Eustathius: Xenodochium in Pontus, 350 A.D.; St. Ephraim: Large emergency hospital in Edessa, 378 A.D., later transferred to Jundi Shapur by the Nestorians; Lady Fabiola, Hospital in Rome and at Ostia, 390 A.D.

foundation of a hospital in Hippo by St. Augustin, then Bishop of Hippo in North Africa (425 A.D.).

East Rome from the division of the Roman Empire (395 A.D.) until the conquest of Byzanz by the Turks in 1453:—The first centuries of the Byzantine Empire were replete with the humanitarian spirit originating from the religious doctrines of the Church. While we hear in the 4th and 5th centuries A.D. almost exclusively of the foundation of hospitals in the East Roman Empire*, we are informed that in the 6th century A.D. under Justinian I (527-567) and his Empress Theodora a health system developed, that branched off in a number of subdivisions and was highly specialized. There were xenodochia (originally sheltering-houses for the poor, the travellers and the sick), orphanotrophia (orphanages), gerontotrophia (homes for the aged), lobotrophia (leper houses), brephotrophia (foundling hospitals), and nosocomia (hospitals). All these institutions were connected with churches or monasteries. The nosocomia were the most important of all. The administration of all branches of medicine was regulated by the Justinian Code.

Subsequent to Justinian I, there was an almost uninterrupted sequence of charitable foundations within the Byzantine Empire. The last ones mentioned in the literature are the hospitals built by the Emperor Isaac I Comnenus (1057-1059), and that erected by the Empress Eirene, wife of John II Comnenus (1118-1143). They are said to have been similar to each other; they were institutions for sick persons under the direction of physicians and in an exemplary way equipped with all the appliances necessary for clinical examination and treatment of patients. The House Rules of Eirene's hospital have been preserved (Byzant. Ztschr., vol.II:628 ff., quoted by Sudhoff, 1913).

There were certainly more such and similar activities within the East Roman Empire in the three last centuries before its final collapse. Internal strife, unbridled luxury and progressive general depravity were, however, highly unfavorable to progress in medical care or even maintenance of previous achievements.

The Church had definitely split in 1054. Whilst the Eastern Church cultivated only one religious order (the Basilians), the Western Church developed

*Emperor Arcadius (395-408): Hospital in Constantinople; Florentinus (in the time of Arcadius): Hospital in Constantinople; Sampson: Famous hospital in Constantinople; Chrysostom of Antioch, later archbishop of Constantinople (see Gibbon, vol.III:302 ff.): Xenodochia at Antioch and Constantinople in 397; Bishop Bassianus: Xenodochium at Ephesus 440 A.D.; Pulcheria, sister of the Emperor Theodosius II (408-450), Emperor Marcianus (450-457), Justus I the Thracian (518-527), Justinian I (527-565) and his general Narses (see Gibbon, vol.IV:189) and Justin II (565-578): Xenodochia, nosocomia, etc. in the East Roman Empire (cf. Baas, 1889; Diehl, 1901; Sudhoff, 1913; Mercher, 1915; Gask and Todd, 1953; Meyer-Steineg and Sudhoff, 1950; Hobson, 1926: part of these with valuable references to sources).

a number of them, almost all of which, particularly the Benedictines, were active in the care of the sick and the needy. The monasteries in which they lived, the institutions which they founded, the hospitals which they erected, were essentially the carriers of medicine and medical service in Western Europe in the Middle Ages*.

The 14th century then brought the erection of hospitals by many cities and towns in Europe and the treatment of their inmates by regular lay-physicians in some of them. This evolutionary process became more and more common in the 16th century and the medical care for the patient at this time was already of paramount importance. Further progress was made when, in the 17th and 18th centuries, medical science advanced theoretically and practically. Not, however, before industrialization on a more and more progressive scale set in, at the middle of the 19th century, did regular and comprehensive medical care of the individual start to be more than either the privilege of the wealthy or the grace of charity. It is today one of the individual's inalienable rights in every civilized country, and he enjoys it in forms different from each other but more or less identical in effect.

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*Three hospitals in Rome, 500 A.D.; Monte Cassino, 529; the Hotel Dieu in Lyons, 542 (the oldest hospital in Europe, still in use); the Hotel Dieu at Arles, early 6th century; the Hospital Merida in Spain, 580; hospitals founded by Pelagius II in Rome (600) and by the Pope Gregory I the Greek (590-604); the Xenodochium in Verdun, mentioned 636 by the Diacon Adalgysus (cf. Virchow, 1860); the hospital in Milano founded late 8th century; the Ospedale di San Spirito in Rome, 8th century; the Hotel Dieu Paris, most probably early 9th century; the Hôpital Mt. Ceniz 825; the Hospital S. Maria della Scalaiin Siena 9th century; the convent-hospital Reichenau, Lake Constance, 9th century; the hospital St. Bernard, 980; the St. Konrad Hospital nr. Constance, 10th century; St. Bartholomew Hospital in London, 1108; the St. Thomas Hospital in England (London, 1200).

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TREATMENT OF ULCERATIVE COLITIS WITH A RESION POLYMYXIN PHTHALYLSULFACETAMIDE PREPARATION

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The complexity of ulcerative colitis from the standpoint of etiology and treatment is well known. The purpose of this writing is not to theorize on the genesis of the disease, nor to review the literature, but to report on a clinical study of a resion, polymyxin, phthalylsulfacetamide preparation (Resion PMS)*. Although ulcerative colitis is a disease of unknown etiology, infection is considered to play an important role. Control of the bacterial flora, bacterial and enteric toxins is desirable. The rationale for this therapeutic approach is based essentially on: 1. lysozyme inhibition, 2. control of enteric pathogens, 3. adsorption of bacterial toxins and of toxic or irritating end-products of digestion and of tissue breakdown.

TABLE I

Stage I	17%	Diffuse hyperemia and friable mucosa on swabbing.
Stage II	25%	Hyperemia, edema and miliary ulceration.
Stage III	33%	Mucopurulent sanguinous exudate, granular, and confluent ulcers.
Stage IV	25%	Confluent ulceration, loss of haustral pattern. Polypoid hyperplasia and structural deformity.

PHARMACODYNAMICS

Resion PMS is a combination of an adsorbive (Resion), consisting of polyamine anion exchange resin, sodium aluminum silicate, and magnesium aluminum silicate with the insoluble antibiotic Polymyxin B as well as the insoluble phthalylsulfacetamide.

Resion was observed to inhibit lysozyme¹, to remove toxic amines², to adsorb bacterial metabolites³. It adsorbs and removes toxic and putrefactive substances from the intestinal tract, having a strong affinity for substances such as indol, skatol, tyramine, putrescine and guanidine which are bound to the insoluble particles of Resion and are removed from the gut without exerting a toxic or irritating effect^{4,5,6}.

Polymyxin is very slightly absorbed and possesses a broad range of activity against the common gram negative enteric pathogens^{7,8}. Virtually no strains develop resistance to Polymyxin⁹. Phthalylsulfacetamide does not produce detectable blood levels¹⁰ when administered orally, and has been found to produce a

*Supplied by National Drug Company, Philadelphia, Pa.

marked fall in bacterial content of the intestinal tract¹¹. With the two in combination, there is a marked synergism against most of the common enteric bacteria¹².

CLINICAL MATERIAL

This is a series of 24 cases of ulcerative colitis in the stages represented in Table I.

The age varied between 12 and 79, as will be noted in Table II. This represents a significant incidence in the sixth and seventh decades.

Except for the acute fulminating case, the severity of symptoms generally was in direct ratio to the duration of the disease.

The minimum follow-up period was four months to well over one year after the resolution of the ulcerative process.

TABLE II
SUMMARY OF STATISTICAL ANALYSIS

Sex	58% Male	42% Female		
Age	25% 10-30 yrs.	42% 30-50 yrs.	33% 50-80 yrs.	
Duration of symptoms	25% 6 mo.-1 yr.	50% 1-5 yrs.	25% 5-15 yrs.	
Number of stools daily	20% 2-6	62% 6-12	18% 12-20	
Bleeding	20% None to occasional	40% Frequent	40% Daily	
Loss in weight	25% 1-10 lbs.	40% 10-20 lbs.	35% 20-40 lbs.	
Abdominal cramps	32% Mild	40% Moderate	28% Severe	

METHOD OF STUDY

Following history, physical examination, and routine laboratory study, each patient was sigmoidoscoped and, in the cases where further evaluation of the more proximal colon was indicated, a barium enema was done. No restriction of diet was imposed, except for the elimination of alcohol. There was no supplementary treatment employed.

Administration of the preparation was in a dosage of one to two tablespoonfuls four times daily depending upon the severity or chronicity of the disease. Medication was given without suggestion of any type regarding its possible effect. The dosage was maintained until either the ulcerative process resolved or insufficient improvement was evident after four weeks to warrant its continuance.

Each patient was followed by sigmoidoscopy at one- to two-week intervals and their progress recorded.

Complete blood count and urinalysis were done periodically. Patients were interrogated as to any unusual reaction. If this were interpreted as due to the medication, omission was advised until symptoms disappeared, and a lower dosage schedule instituted.

CONTROL STUDY

Five patients were used for this study. One patient was represented by stage I, two patients in stage II, and two patients in stage III.

The duration of the disease was from 3 months to 5 years. The remaining statistical data was not dissimilar to the treated group.

These patients were given a placebo simulating Resion PMS in appearance and taste. This was administered for four weeks on the same dosage schedule as the group treated.

Subjective symptoms were essentially unchanged, as was the sigmoidoscopic picture.

TABLE III
RESULTS OF THERAPY

Resolution of ulcerative process	71%
Relapses or residual ulceration	12%
Relatively unchanged or resulting in surgery	17%

RESULTS OF THERAPY

Inasmuch as the number and character of stools, as well as associated symptoms, are variable factors, sometimes not correlated to the pathology, the criteria for improvement were based on endoscopic evaluation of the rectum and sigmoid as well as roentgenologic study. The amount and character of the exudate, as well as the degree of inflammation or ulceration, were the standards by which progress was determined.

Subjective improvement was recorded and assessed but dosage and duration of treatment were determined by the endoscopic picture since symptomatic changes may not be paralleled by changes in the pathology. If there were no symptomatic and pathologic improvement, it was deemed inadvisable to continue the case on this therapy after four weeks.

The results of therapy are briefly summarized in Table III.

In the group in which resolution of the ulcerative process occurred, the time required for the most part varied with the severity of the disease. Table IV shows the time element as compared with the grade of involvement.

Relapses occasionally followed an acute respiratory infection and were controlled by administration of the medication for an average of two to four weeks. The 12 per cent categorized by "relapse or residual ulceration" is a controlled or improved group; however, the effect of the medication is qualified in contrast to those patients whose condition had resolved.

Each case had a follow-up period of at least four months with some cases ranging over one year. There have been some episodes of intermittent moderate diarrhea but not accompanied by changes in the mucosa. The distinction is between a true relapse of the disease as compared with a symptomatic relapse.

There were two instances of apparent intolerance to the drug as manifested by nausea and vertigo. This abated promptly after the omission of the drug which was later well tolerated on a lower dosage schedule. There were no significant changes in routine blood and urine studies.

TABLE IV
TIME REQUIRED IN HEALED CASES

	Per cent	Weeks
Stage I	24	2.5
Stage II	35	4.
Stage III	35	7.1
Stage IV	6	17.

It was interesting to note that in one case of long-standing with a history of unrelenting diarrhea, as well as evidence of marked hyperplastic changes, the patient had only one to two formed stools daily after three weeks of therapy. The persistence of polypoid changes relegated this case to surgery.

SUMMARY AND CONCLUSIONS

Twenty-four patients with ulcerative colitis were treated with a combined preparation of Resion, polymyxin and phthalylsulfacetamide.

Each patient was observed by sigmoidoscopy prior, during, and after therapy. Complete regression of the ulcerative process resulted in 71 per cent while an additional 12 per cent were improved but mucosal resolution was not total. Seventeen per cent were relatively unchanged because of extensive, fulminating disease, or polyposis, and required surgery.

A control study failed to evidence any change in the endoscopic picture and subjective symptoms were essentially unchanged.

It is the sense of the writer, following this clinical study, that Resion PMS adds materially to the armamentarium of therapeutic agents in the treatment of ulcerative colitis.

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EDITORIAL

LIABILITY AT LAW IN GASTROENTEROLOGY

Like the sword of Damocles, the legal threat of a malpractice suit hangs over the physicians and surgeons who are gastroenterologists. It is quite easy for any of us to be sued by a patient. In decades past we were accustomed to hear the expression: "You can't sue the doctor".

In this day and age the calendars of the Supreme Court in one judicial district alone have recorded 203 malpractice actions against physicians, surgeons and dentists. The alarming rise in this type of litigation demands that gastroenterologists be aware of this danger and that the necessary steps be taken to safeguard their particular interests.

It can be stated authoritatively, that the physician and surgeon must use the necessary skill and therapy in the treatment of patients, which skill and therapy is the accepted type and the usual method employed in the community in which he (the physician) resides. Thus, a physician practicing in the backwoods of Kentucky is not required to have the same knowledge, skill and equipment as the university professor attached to a medical center in a large city.

Specifically, the gastroenterologists may fall victims to a legal action under the following circumstances:

1. Using nonaccepted drugs.
2. Improper instrumentation, namely:
 - a. Gastroscopy
 - b. Peritoneoscopy
 - c. Proctosigmoidoscopy
3. Surgical complications during:
 - a. Abdominal paracentesis, for:
 - 1) Treatment
 - 2) Diagnosis
 - b. Abdominal surgery

Gastroenterologists commonly employ new drugs prior to their acceptance by the various agencies designated for that purpose. In the event that a drug is not listed in the standard texts, i.e., United States Pharmacopeia, New and Non-Official Remedies, the National Formulary, etc., there is ground for dispute. If a drug is in the experimental stage and if it is used on a patient, the individual should be apprised of the status of the medication and his permission should be obtained in writing, indicating that he knows the nature of the drug and that he gives written consent to being treated with said drug by his gastroenterologist. One must remember that the "law" deals only in facts, the doctor's

good intention or other moral virtues are of no value in a court of law. Although the physician or surgeon may be prompted by the most noble of motives, the judge and jury are guided only by facts. The facts are that a drug must be acceptable by some accrediting agency prior to its use. Otherwise it is an experimental drug and the patient must give permission to the doctor in writing for administering the drug. Be mindful of the ancient adage: *Cave Legem*.

The utilization of endoscopic procedures for diagnosis and biopsy study has increased a thousand-fold during the last decade. Gastroscopy, peritoneoscopy and proctosigmoidoscopy are the more common forms of instrumentation employed. Of the three, peritoneoscopy is not a completely acceptable standard procedure. A clever lawyer can obtain sufficient expert testimony to disclaim peritoneoscopy as a standard procedure accepted by the medical profession. Therefore, any complication resulting from peritoneoscopy may very easily be classified as negligence. The merits of a case in this type of litigation weighs heavily in the direction of the plaintiff.

Gastroscopy and proctosigmoidoscopy are procedures more readily accepted as standard by the legal experts. A perforation of the esophagus or stomach following gastroscopy, however, is valid cause for an action of negligence against the physician. Similarly, a tear or perforation of the lower bowel following proctoscopic examination is ample cause for instituting legal action against the doctor. Because a legal action is brought against a doctor of medicine does not mean that the plaintiff will win. It does mean endless litigation, waste of time and embarrassment. The plaintiff must prove negligence before the decision is rendered in his behalf.

Abdominal paracentesis performed either for diagnosis or treatment is wrought with the danger of bowel perforation, hemorrhage or shock. For this reason the doctor must protect himself by having the patient sign written permission for this procedure. The doctor must employ diligent care and take all the necessary precautions common to performing a paracentesis by any and all of his professional colleagues in the community in which he practices.

The legal beavers have a field day in attacking the surgeon who does gastroenterologic procedures. Actions have been brought against surgeons, as co-defendants, for acts and omissions of anesthesiologists, nurses and hospitals. The surgeon can be named a co-defendant in mishaps resulting from blood transfusions, infusions, parenteral medication and missing sponges and lap pads. Lawyers have found a new and happier hunting ground in the abdominal surgeon. From the moment he takes a scalpel into his hand, the surgeon is a target for a malpractice action. Such actions have become so common that one may state that the laity find the surgeon the easiest prey to legal blackmail.

Malpractice litigation in recent years has become a thorn in the surgeon's hand. It is well to remember that no malpractice suit can survive without testi-

mony from an opposing surgeon or physician. In truth, many lawsuits can trace their origin to a statement, purposeful or otherwise, made by a physician or surgeon to a patient. Innocent though the remark may be, nevertheless, it plants the seed of suspicion in the patient's mind. After a fertile conversation with a lawyer, the seed blossoms forth as a fruit tree with luscious tasty morsels of money for both the lawyer and his client.

CONCLUSIONS

Attention is called to the ease with which a gastroenterologist may fall victim to a malpractice action.

The legal pitfalls are the use of nonaccepted drugs, instrumentation and surgical procedures.

Properly signed consent authorizations and diligent care are the best means of warding off legal entanglements.

BERNARD J. FICARRA, M.D., LL.B., LL.D., F.A.C.G.

President's Message

The Milwaukee chapter of the American College of Gastroenterology celebrated its 25th anniversary in January of this year. A review of the accomplishments of this group suggests that the addition of more chapters is definitely in line with improving and strengthening our national organization.

The main functions of the American College of Gastroenterology are: the publication of our journal, the annual convention, the postgraduate course, the sponsorship of regional meetings, and encouragement of gastrointestinal research.

The annual convention is a very important effort. Three days of concentrated activity leaves little time for personal contact between members. Discussions of problems of mutual interest among the members of our organization is essential for healthy progress. This is best accomplished on a local or regional level. The formation of additional chapters would definitely fulfill this need, because it would allow for year-round activity and contact among the members.

The Milwaukee chapter has established gastroenterology as a recognized specialty in its locality. Alone, or with allied groups, the chapter has sponsored many excellent scientific programs. With the aid of the national organization the Milwaukee chapter held a regional meeting which was outstanding.

The activities of this group has encouraged young men to enter the field of gastroenterology, and allied specialties. Free discussion of gastrointestinal problems among the members and with invited guests throughout the years has been of inestimable value.

The fear that an individual chapter might dominate the national organization has been largely eliminated. Our constitution provides for the election of members of the board of trustees and the board of governors on a geographical rather than on a numerical basis.

The formation of additional chapters will aid the American College of Gastroenterology in obtaining new members and will strengthen the bonds that unite the present membership.



J. Shaiken

NEWS NOTES

In Memoriam

We record with profound sorrow the passing of Dr. Max Thorek, Chicago, Ill., Fellow and Dr. William L. Bettison, Grand Rapids, Mich., Member of the American College of Gastroenterology. We extend our deepest sympathies to the bereaved families.

APPROVED RESIDENCY IN GASTROENTEROLOGY

An approved residency in gastroenterology is immediately available in a 700-bed general hospital, 45 minutes from New York City. All beds are used for teaching. Applicants must have a minimum of two years' graduate training. Separate service, includes training in all clinical, roentgen and laboratory (research) procedures, esophagoscopy, gastroscopy, etc. Foreign students must have passed the examination of the Educational Council for Foreign Medical Graduates. The stipend is \$300.00 monthly, plus complete maintenance. Applications should be made to the Superintendent, Bergen Pines County Hospital, Paramus, N. J.

VIIITH PAN AMERICAN CONGRESS OF GASTROENTEROLOGY

The VIIth Pan American Congress of Gastroenterology will be held in Santiago, Chile, 23-29 October 1960.

It has been arranged for Delegates to the Congress, who have in their possession regular United States passports, to be admitted as tourists and they will not be required to obtain consular visas. Those who officially represent the United States Government and have been issued special passports, may obtain official visas at the Chilean Embassy in Washington, D. C.

For more detailed information concerning the Congress, please write to Dr. Ricardo Katz U., Secretary-General, Casilla 70-D, Santiago, Chile.

ABSTRACTS FOR GASTROENTEROLOGISTS

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ESOPHAGUS

HAZARDS ATTENDING THE USE OF ESOPHAGEAL TAMPONADE: Harold O. Conn. *New England J. Med.* **259:701** (9 Oct.), 1958.

According to the experience at the Grace New Haven Community Hospital, the complications attending the use of the Sengstaken-Blakemore tube are more frequent, varied and serious than generally recognized. A review of the records and autopsy findings of 50 patients on whom the tube was employed during the period of 1950-1957 was undertaken in order to ascertain how these problems may be prevented or treated.

The tube was used 81 times in 50 patients with an average period of use of 78 hours. In 19 patients major complications arose—9 fatalities directly attributed to its use, and potentially fatal abnormalities during 55 out of 81 episodes of esophageal tamponade. Only 10 patients experienced no difficulty during its use.

The complications associated with the use of the tube are classified as those due to 1. pressure effects, and due to 2. obstruction of the airway.

Obstruction of the airway due to aspiration of foreign material into the bronchia

tree was the most common form of this most serious complication. It is emphasized that the oral nasal and pharyngeal secretions which are in excess of 1,500 ml.; and which cannot longer be swallowed due to obstruction of the upper gastrointestinal tract by the tube, must be removed by suctioning, especially in patients with altered state of consciousness.

It was felt that most of the difficulties encountered were due to lack of experience with the Sengstaken-Blakemore tube. Other less important causes were mechanical defects and sundry incidental factors—A set of rules including: 1. Always use a new tube, 2. Immediately aspirate gastric contents, 3. Avoid use of traction on the apparatus, 4. Avoid oral feedings, 5. Employ constant nursing care, 6. Transect tube before removing to assure deflation of the balloons have been formulated to reduce to a minimum the hazards encountered in the use of this apparatus.

EZRA J. EPSTEIN

STOMACH

INFLUENCE OF DILUTED HYDROCHLORIC ACID UPON THE pH OF GASTRIC CONTENTS: Teppo Vartio and Martti Virtanen. *Ann. med. int. Fenniae* **47:183**, 1958.

Diluted hydrochloric acid (15 drops in a half glass of water) given immediately or

an hour after an ordinary breakfast could not change pH of the gastric contents. The

same amount of hydrochloric acid administered into a fasting stomach caused a drop of pH from 3.0-7.5 to 1.7-2.9 in 6 persons and a change from 4.0-7.4 to 5.4-5.8 in 2 persons 15 minutes after the administration of acid, but this pH lowering effect began to disappear after 30 minutes. The authors

conclude that the beneficial effect of hydrochloric acid sometimes observed in patients with dyspeptic pains cannot be explained by the effect upon the acidity of gastric contents.

SAUL A. SCHWARTZ

HYPOPROTEINEMIA AFTER PARTIAL GASTRECTOMY CORRECTED BY GLUTEN-FREE DIET: John W. B. Forshaw. Brit. M. J. 5103:1020 (25 Oct.), 1958.

The author reports a case of severe impairment of nitrogen absorption following a partial (Polya) gastrectomy. The patient manifested severe glossitis, cheilosis, and angular stomatitis with moderate edema of both legs and a patchy excoriated erythematous rash on the legs and abdomen. He also had four to eight loose stools daily. These symptoms occurred four years after

the operation, and were associated with a severe hypoalbuminemia. The serum albumin returned to normal, and the symptoms completely disappeared on a gluten-free diet, returned when the patient ingested gluten, and disappeared again on a strict gluten-free diet.

SAMUEL M. GILBERT

EVALUATION OF THE SURGICAL TREATMENT OF INTRACTABLE DUODENAL ULCER: Robert M. Zollinger. A.M.A. Arch. Int. Med. 102:607 (Oct.), 1958.

The majority of the surgeons still prefer the two-thirds or three-fourths resection of the stomach followed by gastrojejunostomy. This may be either the Hofmeister anticolonic anastomosis or the Polya retrocolic anastomosis. However, some groups of surgeons recommend vagotomy and gastroenterostomy because of the very low mortality rate especially in poor-risk patients; as in ulcers located near the common duct or in the presence of very extensive inflammatory reaction about the pylorus. Others

prefer to combine vagotomy with pyloroplasty, others with hemigastrectomy, others with a Billroth I procedure. Wangenstein introduced segmental resection. These various methods attempt to reduce the dumping-syndrome as well as the postoperative nutritional failure. However, these sequelae depend only partly on technical factors and are partly due to the patient's personality and his preoperative nutritional status.

H. B. EISENSTADT

THE MEDICAL MANAGEMENT OF PEPTIC ULCER: Carl G. Morlock. A.M.A. Arch. Int. Med. 102:594 (Oct.), 1958.

Five to ten per cent of the entire American population suffer at some time from peptic ulcer. Therefore ulcer therapy is of greatest importance. Two major schools of thought exist with respect to ulcer treatment: 1. depends mainly on rigid diet, antacids, anticholinergics and sedatives, 2. on psychotherapy. The treatment of duodenal ulcer differs somewhat from that of gastric ulcer. Only 15 per cent of all duodenal ulcer cases require surgery while 60 to 70 per cent of all gastric ulcers must be resected. The basis of medical treatment of peptic ulcer is discussed in complete detail.

Gastric ulcer therapy must be extremely

rigid with quarterly x-ray examinations over a period of 18 months. If no healing of the ulcer has occurred after 4 weeks, or if a relapse is noted at any time, resection is indicated. However, partial gastric resection does not protect against gastric carcinoma. Anastomotic ulcers following simple posterior gastroenterostomy may be amenable to a medical regime, while those after partial gastric resection almost always need surgery. Gastric retention due to spasm and edema may be managed medically while that due to scarring requires excisional surgery. Surgical treatment is also preferred for perforation if the patient is seen within the first 24 hours. After this

time a conservative management is preferable. The majority of cases of gastric hemorrhage will be managed medically with early feeding of a Lenhart diet and ade-

quate blood replacement. Intractable ulcer is usually a penetrating ulceration and requires surgical correction.

H. B. EISENSTADT

INTESTINES

GASTROINTESTINAL HEMORRHAGE DURING TREATMENT WITH RAUWOLFIA ALKALOIDS: Janis Gailitis, John B. Nally, Louis E. Burns and Robert B. Motola. *Rhode Island M. J.* 41:546 (Oct.), 1958.

Five cases of gastrointestinal hemorrhage during a two-year period were observed at one hospital, all five receiving the alkaloids in doses at or under 1 mg. reserpine per day.

The five patients were in the sixth decade of life, and were hypertensive, gastrointestinal symptoms, hematemesis and melena were noted after about two years of rauwolfia medication.

Autopsy in one case that died and x-ray studies in the other four revealed gastrointestinal ulceration, concentrated mostly

about the duodenal area.

Experimental evidence is sparse in showing increased gastric secretion under daily doses of 1 mg. reserpine, but these cases are examples in which such secretion occurred.

In using rauwolfia and its compounds, even in normal therapeutic doses any "indigestion" or gastrointestinal uneasiness should be viewed as a danger sign and appropriate steps taken to prevent disasters.

J. EDWARD BROWN

ATYPICAL CONGENITAL MEGACOLON: Edward R. McKay. *J. Internat. Coll. Surgeons* 30:473 (Oct.), 1958.

Hirschprung's disease is an obstruction of the colon due to physiologic inability of peristalsis to propel feces toward the anal opening. The bowel is thickened and leathery, and dilated to 3 or 4 times the normal calibre, up to a point at the rectosigmoid, usually, where the bowel becomes narrowed. It is this narrow part that is dis-

eased, and the defect is the absence of the Auerbach's plexus of nerves. Removal of the narrow section, from the rectosigmoid down to the lower rectum, yields excellent results. A case of unusual interest is reported.

NORMAN L. FREUND

APPENDICITIS IN THE AGED: Erik Christensen. *Brit. M. J.* 5100:832 (4 Oct.), 1958.

Appendicitis is still a serious disease. In spite of the fact that the mortality has fallen, people still die from appendicitis and its complications. In the older age group there has been found a great number of instances of perforation of the appendix. The reason for this is the difficulty in diagnosing appendicitis in the aged. In view of the fact that persons in the older age group have arteriosclerosis, this same process is found in the appendicular ves-

sels with the onset of gangrene more frequent and more rapid than in younger persons. The author reviews appendicitis in patients over 60 and finds that it is not a rare disease in this group. In a study of 1,254 patients 7 per cent were in the older age group. The mortality rate and the rate of complications is quite considerable in patients over 60 with appendicitis.

BERNARD J. FICARRA

CASE OF INFANTILE ULCERATIVE COLITIS: I. Coll and D. Lang Stevenson. *Brit. M. J.* 5102:952 (18 Oct.), 1958.

A case of ulcerative colitis in a 3-week old infant is reported which is considered

to be the youngest patient reported in the literature. Ulcerative colitis in infants runs

a course similar to that of adults, however, it is more severe and interferes with development and growth. Persistent diarrhea with mucus and blood and typical proctoscopic and x-ray findings are noticed in practically every case. Extensive x-ray changes may become apparent in less than two weeks. Medical measures do not differ from those of adults and consist of blood transfusions, parenteral protein, vitamin and electrolyte infusions and steroids. How-

ever, young children never experience the complete remissions seen in adults. Surgery is mandatory for perforation, stricture, arthritis, skin lesions, severe growth failure and malignancy. Left hemicolectomy with anastomosis of the right hemicolon to the terminal rectum had to be performed in the reported infant. This therapy brought about a dramatic improvement.

H. B. EISENSTADT

PREOPERATIVE DIAGNOSIS OF SYMPTOMATIC MECKEL'S DIVERTICULUM:

Richard C. Britton. *Cleveland Clin. Quart.* 24:217 (Oct.), 1958.

Meckel's diverticulum with an incidence as high as 2 per cent has been reported to be the most common congenital gastrointestinal anomaly. Ileal, pancreatic, and gastric tissue may be found in the diverticulum. A patent vitelline duct may extend from the diverticulum to the umbilicus discharging intestinal contents, if present it is more often a solid fibrous cord; obstruction, however, is more often due to local fibrosis and kinking, occasionally to intussusception. Bleeding is correlated with the presence of gastric mucosa, and is due to superficial erosion or to ulcer. Penetration and perforation occur; in Britton's series bleeding occurred more often than diverti-

culitis. In 24 patients reported by Britton, bleeding occurred in 13 patients, diverticulitis in 7, perforation in 2, obstruction in 3. Preoperative diagnosis is difficult or impossible; x-ray examination is practically of no help. A mortality rate of from 6 to 21 per cent has been attributed to delay in diagnosis and operation.

The differential diagnosis concerns the exclusion of other causes of recurrent abdominal pain; peritonitis, intestinal obstruction or rectal bleeding. Britton made a presumptive diagnosis in 9 out of 24 cases. He had no operative mortality. The principal symptoms are pain and bleeding.

SAMUEL L. IMMERMAN

ENDOMETRIOSIS IN COLOPROCTOLOGY: Alfred Solow and Frank Ciampa. *Am. J. Proct.* 9:372 (Oct.), 1958.

Endometriosis is the presence and growth of endometrium-like tissue outside of its normal position lining the uterine cavity. It may be internal, invading the muscle of the uterus (adenomyosis), or external, implanted on the ovary, *cul-de-sac*, bladder, sigmoid, rectum, or rectovaginal septum. In these areas, it will cause periodic swelling and discharge of blood. Sampson's theory of retrograde menstruation through the Fallopian Tubes is the most acceptable means of explanation.

Three of four women have symptoms of dysmenorrhea, sterility, dyspareunia, pain in the pelvis or back, menorrhagia, and discharge of blood from the invaded site at the menses. Constipation and left lower quadrant pain suggest sigmoid involvement. Diagnosis is made by careful history, digital, proctoscopic, and x-ray examination. A nodular tender infiltration in the posterior fornix and a fixed cervix and en-

larged ovary are suggestive. On endoscopy, an extrarectal mass that is tender and irregular is found, but the mucosa is intact. Purplish masses may be seen vaginally. However, the correct diagnosis may not be possible until laparotomy.

Treatment depends on the age and desire for children. Under 40, local excision and fulguration of the lesions is attempted and at least a part of an ovary saved. Over 40, hysterectomy and bilateral oophorectomy is the method of choice. Irradiation is reserved for poor risk patients, those near the menopause, and for the symptomatic recurrences after conservative surgery. When obstruction occurs, resection is carried out in two- or three-stage procedures. Preventive treatment is aimed at subinvolution, retrodisplacements, fibroids, and the avoidance of manipulation and curettage near the menses.

NORMAN L. FREUND

LIVER AND BILIARY TRACT

JAUNDICE OCCURRING IN A PATIENT TREATED WITH CHLOROTHIAZIDE:

A. L. Drerup, W. A. Alexander, George D. Lumb, A. J. Cummins and G. M. Clark. *New England J. Med.* p. 534 (11 Sept.), 1958.

A case report is presented in which chlorothiazide is implicated as a cause of jaundice. The pathological studies from needle biopsy and a wedge resection obtained at exploratory laparotomy were consistent with intrahepatic cholestatic type of jaundice, which has also occurred after therapeutic use of arsphenamine, methyltestosterone, thiouracil, para-aminosalicylic acid, methimazole and chlorpromazine.

After surgery the patient underwent an uneventful convalescence with all liver function studies gradually returning to normal limits within two months.

The patient died on 22 July 1958 from

congestive heart failure. Microscopic examination of the liver revealed nearly complete reversal of the process noted during the episode of jaundice. Occasional foci of necrosis were seen suggesting healing of irregular necrotic areas which may have been caused by some toxic agent although long-standing congestion from heart failure could also have produced comparable findings.

In view of the increasing use of chlorothiazide, clinical awareness should be present of its jaundice producing capabilities.

JOSEPH E. WALTHER

SUBACUTE HEPATIC NECROSIS AND POSTNECROTIC CIRRHOSIS DUE TO ANICTERIC INFECTIONS WITH THE HEPATITIS VIRUS: Gerald Klatskin. *Am. J. Med.* 25:333 (Sept.), 1958.

Nine cases of subacute hepatic necrosis with progression to postnecrotic cirrhosis are described in which the disease appeared to have its inception in an attack of anicteric viral hepatitis. Biopsy material was obtained sufficiently early in the course of the disease to demonstrate the histological features usually considered diagnostic of the infection. Eight out of nine patients were middle aged or elderly women. Characteristically the onset was relatively abrupt with nonspecific constitutional and gastrointestinal complaints. It was followed within a period of two to 18 months by the appearance of frank signs of chronic liver disease. Jaundice was a late development in eight of the nine cases, becoming evident from three to 55 months from the onset. Often it was accompanied by dark urine, light stools, pruritus, and hyperphosphatasemia features that were frequently misinterpreted as evidence of extra-

hepatic biliary obstruction. In addition to the elevated phosphatase, marked hyperglobulinemia, and high levels of thymol turbidity were helpful diagnostic clues. The disease tended to run an intermittently progressive course that was little affected by dietary measures and bedrest, and terminated fatally in five of the nine cases. *Spider nevi* or *Palmar erythema* developed in only two patients. Females at all ages are particularly susceptible to the anicteric form of viral hepatitis that produces subacute hepatic necrosis and postnecrotic cirrhosis. The author suggests that such infections which are readily overlooked or misinterpreted, may be responsible for many instances of otherwise unexplained cirrhosis, and particularly those of the classic postnecrotic variety that occur in females.

JOHN M. McMAHON

Q FEVER WITH LIVER INVOLVEMENT: Charles R. Shuman and John A. Galloway. *Pennsylvania M. J.* 61:1376 (Oct.), 1958.

The authors present a case report of a 60-year old white female diabetic who worked as a handler of goat hair. She developed Q fever as confirmed by a diagnostic antibody titer. The interesting fea-

ture of this case was that this patient had liver involvement as proven by liver biopsy and described by the pathologist as showing "changes of degeneration and inflammation giving support to the clinical diag-

nosis of Q fever". The liver involvement was also confirmed by positive tests for parenchymatous liver disease and hepatomegaly. This patient also had a high pro-

tens OX 19 and typhoid fever titer. This case is of interest in that Q fever is now reported with liver involvement.

RALPH D. EICHORN

CHRONIC SPLENOMEGALY AND ITS RELATION TO HEPATIC PATHOLOGY:

A. K. Basu. *Brit. M. J.* 5102:947 (18 Oct.), 1958.

In India, particularly in Bengal, isolated chronic splenomegaly is a frequently observed disease entity. It is called "tropical" or "Bengal" splenomegaly. The cause is usually unknown, but untreated or insufficiently treated malaria seems to be responsible for the majority of the cases. Such patients lend themselves to the study of the relationship between splenomegaly and hepatic disease, i.e., the Banti's syndrome. Thirty-nine cases were carefully studied with percutaneous or surgical hepatic and splenic biopsy. All cases with chronic congestive splenomegaly characterized by dilatation of the sinusoids, periarterial hemorrhages and erythrophagocytosis were associated with hepatic fibrosis, while in the absence of splenic congestion the liver appeared normal. Therefore, the conclusion was reached that the spleno-

megaly as such is probably not the cause of hepatic disease. However, these patients acquire an independent liver disease especially virus hepatitis quite frequently. This might be due to their decreased resistance in connection with hypersplenism. Then the diseased liver is adversely influenced by the congestive splenomegaly which produces an increased portal flow and pressure just as the hepatic disease affects the existing splenic disease adversely. In order to interrupt the vicious circle created between the two organs, early splenectomy with or without shunt is advised at a time when the hepatic parenchyma is only slightly damaged. Advanced cases will not be benefited by this operation and might even be adversely affected.

H. B. EISENSTADT

CHLORPROMAZINE-TYPE CHOLANGITIS: Richard C. Mechanic and Lawrence Meyers. *New England J. Med.* 259:778 (16 Oct.), 1958.

A very valuable case report indicating that another drug (Phenothiazine derivative) may induce a chlorpromazine type

jaundice. It is reported with blood chemistry, liver profile studies and biopsies.

IRVIN DEUTSCH

CONGENITAL ABSENCE OF THE GALLBLADDER: Jerome J. Weiner. *Am. J. Surg.* 96:724 (Nov.), 1958.

Congenital absence of the gallbladder unassociated with other anomalies of the biliary tract is extremely rare. Embryologically, the biliary tract and liver arise from a ventral outgrowth of the endoderm. The cranial portion gives rise to the liver and bile ducts, while the caudal portion gives rise to the gallbladder and the cystic duct.

The absence of a gallbladder shadow on roentgenological examination may be misinterpreted as representing a pathologic nonfunctioning gallbladder. A diagnosis is rarely made preoperatively.

A case report is given of a 64-year old white woman. The diagnosis of absence of gallbladder was considered preoperatively in this case. Operation revealed no evidence of the gallbladder or cystic duct. The common duct was traced up to the *porta hepatis* and no cystic nubbing or remnant of gallbladder was detected. In spite of the absence of the gallbladder, the patient presented a history typical of gallbladder disease.

CARL J. DEPRIZIO

BOOK REVIEWS FOR GASTROENTEROLOGISTS

LESIONS OF THE LOWER BOWEL: Raymond J. Jackman, M.D., M.S. in Proctology, Section of Proctology, Mayo Clinic and Associate Professor of Proctology, Mayo Foundation, Graduate School, University of Minnesota, Rochester, Minn. 347 pages, illustrated with 75 color plates. Charles C. Thomas, Springfield, Ill., 1958. Price \$15.50.

Dr. Jackman has written a classic in this well printed and illustrated volume on "Lesions of the Lower Bowel". Both black and white and colored illustrations, with adequate explanation, enhance the value for the general practitioner as well as the specialist in internal medicine and the proctologist.

On page 28, etc., the reader will find the positioning of the patient for proctoscopy; the use of instruments. On page 67, the author discusses diagnosis and differential diagnosis of ulcerations of mucosa of the lower bowel. Page 50, *pneumatosis cystoides intestinalis* is described and differ-

ential diagnosis stressed between multiple polyposis and other lesions. Page 160, endometriosis and other extrinsic lesions, which involve the lower bowel, are called to the attention of the physician. Page 175, extrarectal masses in the rectouterine and rectovesical space, call attention to Blumer's shelf and other lesions and proctoscopy of these patients.

The color atlas is a valuable addition. The author and publisher are to be commended for this valuable work. It is highly recommended to medical students and to all physicians.

TREATMENT IN INTERNAL MEDICINE: Harold Thomas Hyman, M.D., Diplomate, American Board of Medicine, Consulting Physician, Monmouth Memorial Hospital, Long Branch, Riverview Hospital, Red Bank, N. J., Formerly Assistant Professor of Pharmacology, Columbia University, Associate Attending Physician, The Mt. Sinai Hospital, New York, N. Y., Attending Physician, The Montefiore Hospital, New York, N. Y., with a foreword by Walter C. Alvarez, M.D. 609 pages, illustrated in color and black and white. J. B. Lippincott Company, Philadelphia, Pa., 1958. Price \$12.50.

Twenty-seven chapters are subdivided into 10 sections, all crammed full of up to date useful nuggets. The reviewer cannot but marvel at the amount of information which Dr. Hyman assembled into this well

written, printed and beautifully executed volume.

The reviewer received great satisfaction from reading this book and recommends it highly.

MUIR'S TEXTBOOK OF PATHOLOGY—SEVENTH EDITION: Revised by D. F. Cap-
pell, C.B.E., M.D., F.R.P.S., M.R.C.P., F.R.S. Ed., Professor of Pathology, University of Glasgow; Pathologist to the Western Hospitals Group, Glasgow; Consultant Pathologist to the Western Regional Group. 1201 pages, many illustrations. Edward Arnold, Ltd., London; The Williams & Wilkins Co., Baltimore, Md., 1958. Price \$14.50.

When a text reaches seven editions, undoubtedly it has gained the approval of the medical profession.

Not only is the contents of the volume up to date, but it also adds historical notes which enhance the description of the pathological basis and original observations of previous clinicians. On page 100, there is an interesting notation regarding the introduction of syphilis into Europe. Infection, fever, immunity is worthwhile reading, as well as tumors and their classification. Discussion of the circulatory, respira-

tory and gastrointestinal systems are well written and illustrated. In fact, the entire volume is a gem.

Many students and physicians preparing for specialty boards are urged to read and memorize the various illustrations of tissues, because they may find them of value when microscopic slides are part of the examination.

Bibliography and a comprehensive index are included.

It is highly recommended and should be of great value to all.

CLINICAL CHEMISTRY IN PRACTICAL MEDICINE: C. P. Stewart, D.Sc. (Dunelm), Ph.D. (Edin.), Reader in Clinical Chemistry, University of Edinburgh, Senior Biochemist, Royal Infirmary, Edinburgh and D. M. Dunlop, B.A. (Oxon), M.D., F.R.C.P. (Edin.), F.R.C.P. (London), Christison Professor of Therapeutics and Clinical Medicine, University of Edinburgh, Physician, Royal Infirmary, Edinburgh. 342 pages. E. & S. Livingstone Ltd., Edinburgh and London. Williams & Wilkins Co., Baltimore, Md., 1958. Price \$6.75.

Appendix 1 and appendix 2, plus an index, add to the usefulness of this concise text.

Chapter by chapter it elucidates the

whys and wherefors of the tests, etc.

Medical students and graduates preparing for Board examinations will find this little volume of value.

INSULIN TREATMENT IN PSYCHIATRY: Max Rinkel, M.D. and Harold E. Himwich, M.D. 386 pages. Philosophical Library, New York, N. Y., 1959. Price \$5.00.

Based on Dr. Sakel's use of insulin in patients who required shock treatment, it is interesting reading and instructive, as the reader may note on page 17, . . . insulin treatment is the standard method of choice for paranoid schizophrenia. This treatment may be enhanced by introducing electric or cardiazol (metrazol) shock treat-

ment during the cure, plus psychotherapy.

Page 231, indications for insulin therapy is worthwhile reading.

It is recommended that this book should be read by physicians, as it will give them a better understanding what shock therapy, whether by insulin or other agents, can do to rehabilitate many hopeless cases.



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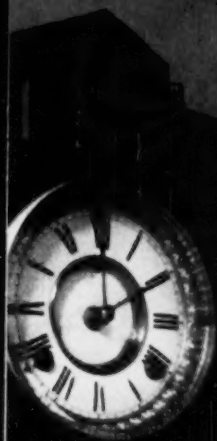
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1. *British Medical Journal* 2:827, 1955
2. *American Journal of Gastroenterology* 28:439, 1957



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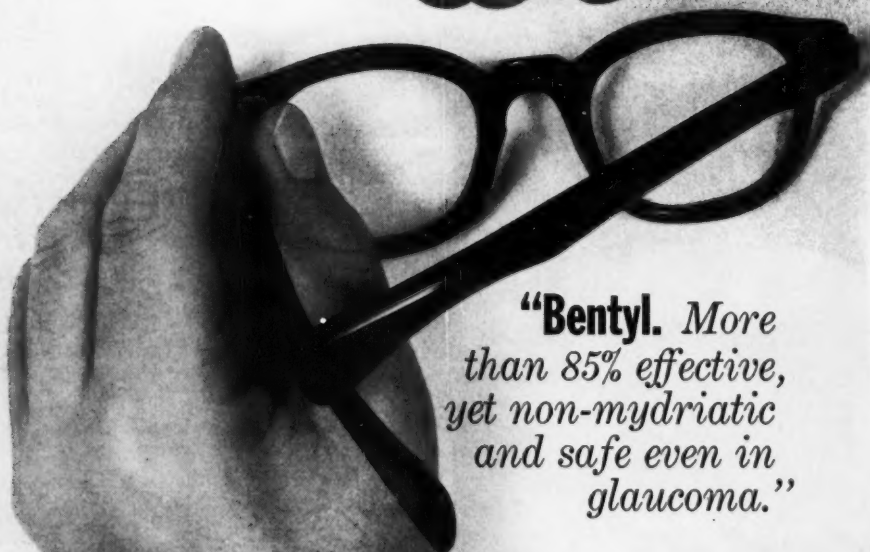
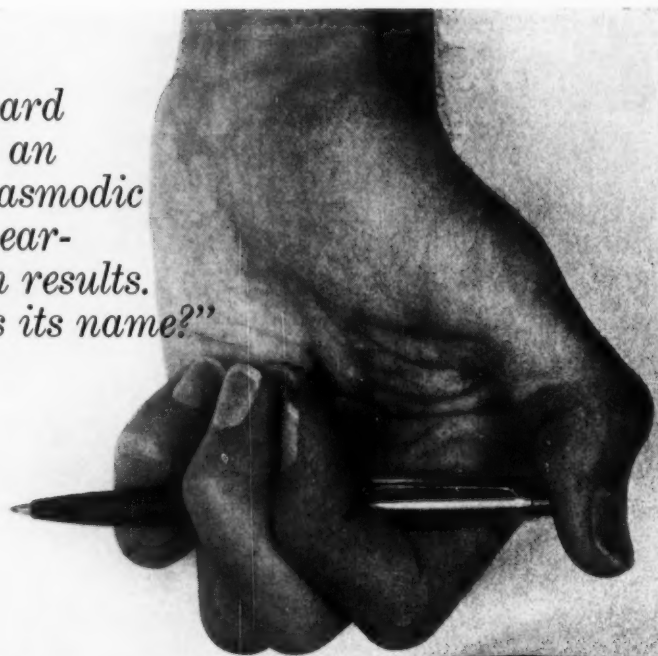
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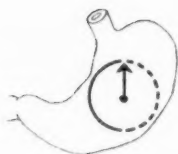
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1. *Can. J. Med. Sci.* 50: 1429-1434 (Sept. 1955). 2. *Report B. J. Annals of the Royal College of Physicians*, London, 1955. 3. *British Medical Journal*, London, 1955. 4. *British Medical Journal*, London, 1955. 5. *British Medical Journal*, London, 1955. 6. *British Medical Journal*, London, 1955. 7. *British Medical Journal*, London, 1955. 8. *British Medical Journal*, London, 1955. 9. *British Medical Journal*, London, 1955. 10. *British Medical Journal*, London, 1955.

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1. Nesselrod, J. P.: *Clinical Proctology*, ed. 2, Philadelphia, Saunders, 1957. 2. Page, S. G., Jr., et al.: *J. A. M. A.* 157:1208, Apr. 2, 1955. 3. Gross, J. M.: *J. Internat. Coll. Surgeons* 23:34, Jan., 1955. 4. Page, S. G., Jr., et al.: *Gastroenterology* 32:747, Apr., 1957. 5. Hellman, L. D.: To be published.

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1. Hinkel, E. T., Jr.; Fisher, M. P., and Tainter, M. L.: *J. Am. Pharm. A. (Scient. Ed.)* 48:380, July, 1959. 2. Hinkel, E. T., Jr.; Fisher, M. P., and Tainter, M. L.: *J. Am. Pharm. A. (Scient. Ed.)* 48:381, July, 1959.

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REFERENCES: 1. Ayd, F. J., Jr.: *Current Therapeutic Research* 1:41 (Oct.) 1959. 2. Recent compilation of case reports received by the Medical Department, White Laboratories, Inc.

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Galeota, W. R., and Moranville, B. A.: Student Medicine (in press)

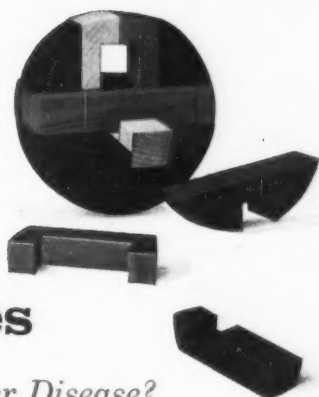
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1. Cook, J.E., Briggs, G.W., and Hindley, F.W.: Chronic Amebiasis and the Need for a Diagnostic Profile, *Am. Pract. and Dig. of Treat.* 6:1821 (Dec., 1955).

2. Rinehart, R.E., and Marcus, H.: Incidence of Amebiasis in Healthy Individuals, Clinic Patients and Those with Rheumatoid Arthritis, *Northwest Med.* 54:708 (July, 1955).

3. Webster, B.H.: Amebiasis, a Disease of Multiple Manifestations, *Am. Pract. and Dig. of Treat.* 9:897 (June, 1958).

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